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(44) THE: SUBSITIVIED POLYCYCLIC ARYL AND HETEROARYL PYRIDINES USEFUL FOR SELECTIVE INHIBITION OF THE COADULATION CASCADE

(\$7) Abstract. The present invention relates to compounds, and prodrugs thereof, composition and methods useful for preventing and treating thrombotic conditions in mammals. The compounds of the present invention, and prodrugs thereof, selectively inhibit certain proteases of the coagulation cascade

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SUBSTITUTED POLYCYCLIC ARTH AND HETEROARYL-PYRIDINES USEFUL FOR SELECTIVE INHIBITION OF THE COAGULATION CASCADE

Field of the Invention

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therapy, and specifically relates to compounds, compositions conditions such as coronary artery and cerebrovascular disease. More particularly, the invention relates to This invention is in the field of anticoagulant compounds, and prodrugs thereof, that inhibit serine substituted polycyclic aryl and heteroaryl pyridine and methods for preventing and treating thrombotic proteases of the coagulation cascade.

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Background of the Invention

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Book Co., pp. 348-351]. The normal hemostatic system limits and plasma proteins. However, unregulated activation of the platelets aggregate to form the primary hemostatic plug and Hemorrhage, intravascular thrombosis, and embolism are components of the vessel wall, circulating blood platelets, of common clinical manifestations of many diseases [see R. I. Wilson, et al. eds., 12th ed. 1991) New York, McGraw-Hill platelets first adhere to macromolecules in subendothelian fluid within the vascular systems and yet quickly be able undergo hemostasis. Hemostasis, or clotting, begins when McGraw-Hill Book Co., pp. 1341-1343]. Blood must remain stimulate local activation of plasma coagulation factors of the hemostatic system may cause thrombosis, which can myocardium. Physiological systems control the fluidity Gilman's The Pharmacological Basis of Therapeutics (J.G. reduce blood flow to critical organs like the brain and regions of injured and/or damaged blood vessels. These blood in mammals [see P.W. Majerus, et al. in <u>Goodman &</u> blood loss by precisely regulated interactions between Hardman & L.E. Limbird, eds., 9th ed. 1996) New York, Handin in Harrison's Principles of Internal Medicine

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leading to generation of a fibrin clot that reinforces the aggregated platelets.

plasma coagulation factors, also referred to as protease zymogens, include factors II, V, VII, VIII, IX, X, XI, and XII. These coagulation factors or protease zymogens are activated by serine proteases leading to coagulation in a so called "coagulation cascade" or chain reaction.

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Coagulation or clotting occurs in two ways through different pathways. An intrinsic or contact pathway leads from XII to XIIa to XIa to IXa and to the conversion of X to Xa. Xa with factor Va converts prothrombin (II) to thrombin (IIa) leading to conversion of fibrinogen to fibrin. Polymerization of fibrin leads to a fibrin clot. An extrinsic pathway is initiated by the conversion of coagulation factor VII to VIIa by Xa. Factor VIIa, a plasma protease, is exposed to, and combines with its essential cofactor tissue factor (TF) which resides constitutively beneath the endothelium. The resulting factor VIIa/TF complex proteolytically activates its substrates, factors IX and X, triggering a cascade of reactions that leads to the generation of thrombin and a fibrin clot as described above.

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while clotting as a result of an injury to a blood vessel is a critical physiological process for mammals, clotting can also lead to disease states. A pathological process called thrombosis results when platelet aggregation and/or a fibrin clot blocks (1.e., occludes) a blood vessel. Arterial thrombosis may result in ischemic necrosis of the tissue supplied by the artery. When the thrombosis occurs in a coronary artery, a myocardial infarction or heart attack can result. A thrombosis occurring in a vein may cause tissues drained by the vein to become edematous and inflamed. Thrombosis of a deep vein may be complicated by a pulmonary embolism. Preventing or treating clots in a blood vessel may be therapeutically useful by inhibiting formation of blood platelet aggregates, inhibiting formation of

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fibrin, inhibiting thrombus formation, inhibiting embolus formation, and for treating or preventing unstable angina, refractory angina, myocardial infarction, transient ischemic attacks, atrial fibrillation, thrombotic stroke, embolic stroke, deep vein thrombosis, disseminated intravascular coagulation, ocular build up of fibrin, and reocclusion or restenosis of recanalized vessels.

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In order to treat such conditions, researchers have sought to discover chemical compounds that efficaciously and selectively control the clotting process. In addition, such compounds may provide a better understanding of the pathways involved in the coagulation process.

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Thus far, many of the compounds that have been discovered possess a polar or basic functional group which is integrally responsible for the desired biological activity. Frequently, this polar functional group is a nitrogen atom of, for example, a guandine, alkyl-amidine or aryl-amidine group. Because these functionalities are highly basic, they remain protonated at physiologically relevant pH's. The ionic nature of such protonated species hinders their permeability across lipophilic membranes, which can reduce bioavailability when the pharmaceutical agent is administered orally.

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In order to circumvent such a problem, it is often advantageous to perform a derivatization or chemical modification of the polar functionality such that the pharmaceutical agent becomes neutrally charged and more lipophilic, thereby facilitating absorption of the drug. However, for the derivatization to be useful, the derivatization must be bioconvertable at the target site or sites of desired pharmacological activity and cleaved under normal physiological conditions to yield the biologically active drug. The term "prodrug" has been used to denote such a chemically modified intermediate.

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There have been limited reports of non-peptidic and peptidic pyridine compounds that act as an inhibitor of a

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Summary of the Invention

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inhibition of certain enzymes that act upon the coagulation Among the objects of the present invention, therefore, is the provision of compounds useful for selective cascade thereby preventing and treating thrombotic conditions in mammals.

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undergo hydrolysis, oxidation, reduction or elimination at a inhibition of certain enzymes that act upon the coagulation conditions in mammals. In general, these prodrug compounds derivatized amidine group to yield the active compound. provision of prodrug compounds useful for selective Another object of the present invention is the cascade thereby preventing and treating thrombotic

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to the compound, per se, to the prodrug of the compound, to Briefly, therefore, the present invention is directed prodrug and a pharmaceutically acceptable carrier, and methods of use. The compound corresponds to Formula A: pharmaceutical compositions comprising the compound or

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Naylor-Olsen et al. describe disubstituted benzenes having a

JS Patent 5,872,138 and PCT Patent Application WO 98/10763,

neteroatom, any one of six basic heterocycles linked to the

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group linked through an oxygen, nitrogen or sulfur

alkyl, alkenyl, alkoxy, amino, or arylmethylenesulfonamido

ring through linker group, and, optionally, an additional

group and claimed to inhibit human thrombin. In PCT Patent

groups and having inhibitory activity against factor Xa. In

alkoxy, acetamide, carbonates, carbamates, ureas, and other

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substituents that include acylamido, acyloxy, carboxamido,

et al. describe benzenes that may be fully substituted by

PCT Patent Applications WO 99/00121 and WO 99/00128, Beight

substituted aminos and reported to be inhibitors of trysin-

difluoro pyrid-2-ylacetamides that are further substituted

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it the 6-position by several groups including several

dichloro, 3-fluoro-5-chloro, 3-chloro-5-fluoro, and 3,5-

Wexler et al. describe certain 3,5-unsubstituted, 3,5-

clotting process. In PCT Patent Application WO 00/039102, coagulation factor present in the coagulation cascade or

thrombin. There have been reports of non-peptidic benzene compounds that act as an inhibitor of a coagulation factor present in the coagulation cascade or clotting process. In

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like serine protease enzymes, especially factor Xa and

Formula A

wherein

 $X_1,\ X_2,\ X_3\ X_4,\ X_5,$ and X_6 are each ring atoms defining a 6 membered heterocyclic or aromatic ring;

X1, X2, and X4 are independently carbon or nitrogen; X, is carbon;

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utility as inhibitors of thrombotic disorders. In PCT Patent

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Application WO 96/40100, Illig et al. describe sulfonamido

directed to non-peptidic factor Xa and claimed to have

utility as inhibitors of thrombotic disorders.

substitutedbenzoyl and benzyl derivatives of amines

substitutedbenzoyl) derivatives of diamines claimed to have

WO 96/39380, Lu and Soll describe bis-(sulfonamido

naving activity against thrombin.

In PCT Patent Application

unction in the group substituting the amide nitrogen and

2,3,4,5-tetrasubstitutedphenylacetamides having an acyl

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Application WO 99/26920, Semple et al. disclose 1-oxy-

sulfur, provided at least one of X_1 , X_4 , and X_6 is other than X, and X, are independently carbon, nitrogen, oxygen or carbon when X2 is carbon;

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 X_1 , Z_3 is covalently bonded to X_3 , and Z_4 is covalently bonded $X_1,\ X_2,\ X_3,\ X_4,\ X_5,\ and\ X_6,\ wherein\ Z_1$ is covalently bonded to respectively, are covalently bonded to different ring atoms and Z_{i} are covalently bonded to $X_{1},\ X_{3}$ and $X_{4},\ respectively;$ $L_{1},\ L_{3}$ and L_{4} are linkages through which $Z_{3},\ Z_{3},\$ and $Z_{4},$ of the 6 membered heterocyclic or aromatic ring defined by to X_{i} , each of L_{i} , L_{j} and L_{i} independently being a covalent bond or comprising one or more atoms through which $\mathbf{Z_{1}},\ \mathbf{Z_{1}},$

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ring is optionally substituted at any position with halogen. of the hydrocarbyl or ring comprising an amidine, guanidine Z, is a substituted hydrocarbyl, or a 5 or 6 membered substituted heterocyclic or aromatic ring, the substituents nembered heterocyclic or aromatic ring of Z, being carbon, amino, or aminoalkyl group, the ring atoms of the 5 or 6 sulfur, nitrogen, or oxygen, wherein the 5 or 6 membered hydroxy, or alkyl;

 $\mathbf{Z}_{\mathbf{t}}$ comprises hydrocarbyl, substituted hydrocarbyl or a 5 or 6-membered heterocyclic ring, the ring atoms of the 5 or 6-membered heterocyclic ring being carbon, sulfur, nitrogen or oxygen;

 $\mathbf{z_i}$ is hydrogen, hydrocarbyl, or substituted hydrocarbyl;

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 \mathbf{Z}_{2} is a hydrogen bond acceptor covalently or datively

Other objects and features of this invention will be in part apparent and in part pointed out hereafter. bonded to X2.

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DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Formula I Embodiment

In one embodiment, the present invention is directed to compounds of Formula (I) (which constitute a subset of the compounds of Formula (A)):

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M is selected from the group consisting of N and $N \! \rightarrow \! 0$; or a pharmaceutically acceptable salt thereof, wherein; B is formula (V):

when two of $D^1,\ D^2,\ J^3,\ J^2$ and K^1 are O and S, and no more than four of $D^1,\ D^2,\ J^1,\ J^2$ and K^1 are N, with the provisos that $D^1,$ independently selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of $\mathbf{J}^1,~\mathbf{J}^2$ and \mathbf{K}^1 is S, one of $\mathbf{D}^1,~\mathbf{D}^2,~\mathbf{J}^1,~\mathbf{J}^2$ and \mathbf{K}^1 must be a bond one of D¹, D², J¹, J² and K¹ is O, no more than one of D¹, D², wherein $D^1,\ D^2,\ J^1,\ J^2$ and K^1 are independently selected from provisos that no more than one can be a bond, no more than D^2 , J^1 , J^2 and K^1 are selected to maintain an aromatic ring the group consisting of C, N, O, S and a bond with the system and that $R^{12},\ R^{13},\ R^{34},\ R^{35},$ and R^{36} are each sulfur, and the divalent nature of oxygen;

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and R36 are independently selected from the group consisting R9, R10, R11, R12, R13, R16, R17, R18, R19, R32, R31, R31, R35, heterocyclylamino, heterocyclylalkylamino, hydrido, acetamido, haloacetamido, amidino, guanidino, of heterocyclylalkoxy, N-alkyl-N-arylamino,

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aryloxyalkyl, saturated heterocyclyl, partially saturated

haloalkoxyalkyl, aryl, aralkyl, aryloxy, aralkoxy,

aralkylaryl, aralkyl, aralkenyl, aralkynyl, heterocyclyl, aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, acylalkyl, acylalkoxy, aryloylalkoxy, heterocyclyloxy, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, haloalkoxylalkyl, heteroaralkoxy, cycloalkylamino, dialkylsulfoniumalkyl, carboxy, heteroaralkylthio, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, dialkylsulfonium, trialkylphosphonium, halocycloalkenyl, cycloalkylsulfinyl,

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cycloalkylgulfonylalkyl, heteroarylamino, N-heteroarylaminocycloalkenyloxyalkyl, cycloalkylenedioxy, halocycloalkoxy, heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, halocycloalkenyloxyalkyl, hydroxy, amino, alkoxyamino, cycloalkenyloxy, cycloalkoxyalkyl, cycloalkylalkoxy, thio, nitro, alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl N-alkylamino, heteroaralkylamino, cycloalkoxy, cycloalkylsulfinylalkyl, cycloalkylsulfonyl, halocycloalkoxyalkyl, halocycloalkenyloxy,

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lkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfinylalkyl, heteroarylsúlfinylalkyl, heteroarylsulfonylalkyl, naloalkylsulfonylalkyl, alkylsulfonamido, arylsulfinylalkyl, arylsulfonylalkyl,

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neterocyclylsulfonyl, heterocyclylthio, alkanoyl, alkenoyl, amidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl haloalkanoyl, alkyl, alkenyl, alkynyl, alkenyloxy, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, alkenyloxyalky, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkylalkanoyl, cycloalkenyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, heteroarylsulfinyl, heteroarylsulfonyl, 25 30

haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl,

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ydroxyalkyl, alkylenylamino, hydoxyheteroaralkyl,

cycloalkylalkyl, cycloalkenylalkyl, halo, haloalkyl,

R' and R10, R10 and R11, R11 and R12, or R12 and R13 is bonded heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, together to form a ring selected from the group consisting members, a heteroaryl ring having 5 through 6 members, and members, a partially saturated heterocyclyl ring having 5 partially saturated heterocyclyl ring having 5 through 8 through 8 members, a heteroaryl ring having 5 through 6 R12 and R31, R33 and R34, R34 and R35, or R35 and R36 is R16, R19, R12, R13, R14, R15, and R16 are independently bonded together to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8 of a cycloalkenyl ring having 5 through 8 members, a carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl; heteroarylalkyl, arylalkenyl, heteroarylalkenyl, alkylamidocarbonylamido, arylamidocarbonylamido, carboalkoxyalkyl, carboalkoxyalkenyl, carboxy, carboxyalkyl, carboalkoxy, alkoxycarboxamido, carbohaloalkoxy, phosphono, phosphonoalkyl, B is optionally formula (VI): members, and an aryl; optionally Qb; 10 12 20 52

wherein D³, D⁴, J³, and J⁴ are independently selected from the group consisting of C, N, O, and S, no more than one of D^{J} , D', J', and J' is O, no more than one of D', D', J', and J' is

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S, and no more than three of D^1 , D^2 , J^1 , and J^2 are N, with the provisos that D^3 , D^4 , J^2 , and J^4 are selected to maintain an aromatic ring system and that R^{22} , R^{23} , R^{24} , and R^{25} , and R^{36} are each independently selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen;

B is optionally selected from the group consisting of hydrido, trialkylsilyl, C2-C8 alkyl, C3-C8 alkenyl, C3-C8 alkylenyl, C3-C8 alkynyl, C2-C8 haloalkyl, and C3-C8 haloalkenyl wherein each member of group B is optionally substituted at any carbon up to and including 6 atoms from the point of attachment of B to A with one or more of the group consisting of R₃₁, R₃₄, R₃₅, and R₃₆;

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the point of attachment is optionally substituted with $R^{10},\ a$ ring carbon or nitrogen atom adjacent to the \mathbb{R}^{13} position and position is optionally substituted with R¹¹, a ring carbon or provided that no more than one ring carbon is substituted by nitrogen atom adjacent to the R' position and two atoms from B is optionally selected from the group consisting of R33, and a ring carbon or nitrogen atom four atoms from the point of attachment and adjacent to the R11 and R13 positions wherein each ring carbon is optionally substituted with $\mathbb{R}^{33},$ nitrogen atom three atoms from the point of attachment and adjacent to the R12 position is optionally substituted with atoms from the point of attachment and adjacent to the $R^{10}\,$ substituted with R12, a ring carbon or nitrogen atom three adjacent to the carbon atom at the point of attachment is heterocycly1, and C4-C9 partially saturated heterocycly1, C3-C15 cycloalkyl, C5-C10 cycloalkenyl, C4-C12 saturated a ring carbon other than the ring carbon at the point of attachment of B to A is optionally substituted with oxo optionally substituted with R° or R13, a ring carbon or two atoms from the point of attachment is optionally oxo at the same time, ring carbon and nitrogen atoms is optionally substituted with R34;

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A is selected from the group consisting of a bond, (W⁷)_{rr}-(CH(R¹³))_{ps}-(W⁷)_{rr} wherein rr is an integer selected from 0 through 1, ps is an integer selected from 0 through 6, and W⁷ is selected from the group consisting of 0, S, C(O), C(S), C(O)S, C(S)O, C(O)N(R⁷), C(S)N(R⁷), (R⁷)NC(O), Se(O), N(R⁷), (R⁷)NS(O), (R⁷)NC(NR⁷), (R⁷)NC(NR⁷), (R⁷)NC(NR⁷), (R⁷)NC(NR⁷) NR⁷, and N(R⁷) with the proviso that no more than one of the group consisting of rr and pa is 0 at the same time; R⁷ and R⁸ are independently selected from the group .

R' and R' are independently selected from the group .
consisting of hydrido, hydroxy, alkyl, alkenyl, aryl,
aralkyl, aryloxy, alkoxy, alkenyloxy, alkylthio, alkylamino,
arylthio, arylamino, acyl, aroyl, heteroaroyl,
aralkoxyalkyl, heteroaralkoxyalkyl, aryloxyalkyl,
alkoxyalkyl, alkenyloxyalkyl, alkylthioalkyl,
aralkoxyalkyl, heteroaralkoxyalkyl, alkylsulfinylalkyl,
alkylsulfonylalkyl, heteroaryl, heteroaryloxy,
heteroarylamino, heteroaralkyl, heteroaralkyloxy,
heteroaralkylamino, and heteroaryloxyalkyl;

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selected from the group consisting of amidino, hydroxyamino, halocycloalkenyloxyalkyl, saturated heterocyclyl, partially alkoxy, alkylthio, arylthio, alkyl, alkenyl, alkynyl, aryl, alkenyloxyalkyl, alkylthioalkyl, arylthioalkyl, cycloalkyl, haloalkenyloxyalkyl, halocycloalkoxy, halocycloalkoxyalkyl, R14, R15, R37, R38, R39, R40, R41 and R42 are independently hydrido, hydroxy, halo, cyano, aryloxy, amino, alkylamino, cycloalkenylalkyl, haloalkyl, haloalkenyl, halocycloalkyl, heteroaralkoxythioalkyl, alkoxyalkyl, heteroaryloxyalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, aralkylthioalkyl, heteroaroyl, heteroaryloxyalkyl, sulfhydryl, acylamido, saturated heterocyclyl, heteroaryl, heteroarylalkyl, dialkylamino, hydroxyalkyl, aminoalkyl, acyl, aroyl, cycloalkylalkyl, cycloalkylalkenyl, cycloalkenyl, halocycloalkenyl, haloalkoxy, haloalkoxyalkyl, aralkyl, aryloxyalkyl, aralkoxyalkylalkoxy,

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monocarboalkoxyalkyl, dicarboalkoxyalkyl, monocyanoalkyl, heteroarylthioalkyl, heteroaralkylthioalkyl,

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alkylsulfonyl, haloalkylsulfinyl, haloalkylsulfonyl, dicyanoalkyl, carboalkoxycyanoalkyl, alkylsulfinyl,

arylsulfonylalkyl, aralkylsulfinyl, aralkylsulfonyl, arylsulfinyl, arylsulfinylalkyl, arylsulfonyl

cycloalkylsulfinylalkyl, cycloalkylsufonylalkyl, cycloalkylsulfinyl, cycloalkylsulfonyl,

heteroarylsulfonyl, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, heteroarylsulfinyl, 10

carboxyalkyl, carboalkoxy, carboxamide, carboxamidoalkyl, aralkylsulfinylalkyl, aralkylsulfonylalkyl, carboxy, carboaralkoxy, trialkylsilyl, dialkoxyphosphono,

oxoacyl and \mathbb{R}^{19} is optionally substituted at from one through three of the ring carbons with a substituent selected from diaralkoxyphosphonoalkyl, with the proviso that R^{17} and R^{18} are independently selected from other than formyl and 2diaralkoxyphosphono, dialkoxyphosphonoalkyl, and

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optionally bonded together to form a group selected from the R14 and R14, when bonded to different carbons, are the group consisting of R16, R17, R18, and R19;

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members, cycloalkenyl ring having from 5 through 8 members, group consisting of a bond, alkylene, haloalkylene, and spacer selected to form a ring selected from the group consisting of cycloalkyl ring having from 5 through 8

and a heterocyclyl having from 5 through 8 members;

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group consisting of a cycloalkyl ring having from 5 through optionally bonded together to form ring selected from the members, a cycloalkenyl ring having from 5 through 8 R14 and R15, when bonded to different carbons, are nembers, and a heterocyclyl having from 5 through 8 nembers;

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group consisting of cycloalkyl ring having from 5 through 8 optionally bonded together to form a ring selected from the R15 and R15, when bonded to different carbons, are

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members, cycloalkenyl ring having from 5 through 8 members, and a heterocyclyl having from 5 through 8 members;

C(0), C(S), S(0), S(0), O(0), $O(R^5)$, O(0)\Psi is selected from the group consisting of NR\$, 0,

alkoxyalkyl, alkenyloxyalkyl, alkylthioalkyl, arylthioalkyl, aryloxy, aralkoxy, alkoxy, alkenyloxy, alkylthio, arylthio, haloalkoxyalkyl, haloalkenyloxyalkyl, halocycloalkoxyalkyl, haloalkyl, haloalkenyl, halocycloalkyl, halocycloalkenyl, R5 is selected from the group consisting of hydrido, aralkoxyalkyl, heteroaralkoxyalkyl, alkylsulfinylalkyl, hydroxy, amino, alkyl, alkenyl, alkynyl, aryl, aralkyl, halocycloalkenyloxyalkyl, heteroaryl, heteroarylalkyl, cycloalkylalkenyl, cycloalkenyl, cycloalkenylalkyl, aralkoxyalkyl, heteroaralkoxyalkyl, aryloxyalkyl, alkylsulfonylalkyl, cycloalkyl, cycloalkylalkyl,

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monocarboalkoxyalkyl, monocarboalkoxy, dicarboalkoxyalkyl, carboalkoxycyanoalkyl, acyl, aroyl, heteroaroyl, heteroaryloxyalkyl, and dialkoxyphosphonoalkyl; nonocarboxamido, monocyanoalkyl, dicyanoalkyl,

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optionally bonded together to form a group selected from a haloalkylene, and a spacer having from 2 through 7 atoms and a to form a ring selected from the group consisting of cycloalkenyl ring having from 3 through 8 members, cycloalkyl ring having from 3 through 8 members, a R19 and R40, when bonded to the same carbon, are group consisting of exe, thione, R'-N, alkylene, heterocyclyl ring having from 3 through 8

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Ja is independently selected from the group consisting of N and C-Xº;

Jb is independently selected from the group consisting of N and C-R1;

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 $R^2,\ R^1,\ and\ X^o$ are independently selected from the group of N and C-R';

Jc is independently selected from the group consisting

consisting of Z°-Q, hydrido, alkyl, alkenyl, and halo;

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R' and X° are independently optionally selected from the haloalkoxy, haloalkylthio, amino, alkylamino, aminoalkyl, amidino, guanidino, hydroxy, hydroxyamino, alkoxy, group consisting of amino, aminoalkyl, haloalkyl, hydroxyalkyl, alkoxyamino, thiol, alkylthio, dialkylsulfonium, trialkylphosphonium,

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dialkylsulfoniumalkyl, heteroarylamino, nitro, arylamino, aralkylamino, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl,

 \mathbb{R}^2 is optionally selected from the group consisting of hydroxyhaloalkyl, cyano, and phosphono;

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amidino, guanidino, dialkylsulfonium, trialkylphosphonium, alkylamino, arylamino, aralkylamino, alkanoyl, alkenoyl, haloalkanoyl, hydroxyhaloalkyl, cyano, and phosphono; dialkylsulfoniumalkyl, heteroarylamino, amino, nitro, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl,

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consisting of a heteroaryl ring having from 5 through 6 X° and R¹ are optionally selected to be -W=X-Y=Zwherein -W=X-Y=Z- forms a ring selected from the group members and an aryl;

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consisting of a heteroaryl ring having from 5 through 6 wherein -W=X-Y=Z- forms a ring selected from the group R¹ and R² are optionally selected to be -W=X-Y=Zmembers and an aryl;

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group consisting of $C(R^9)$, $C(R^{10})$, $C(R^{11})$, $C(R^{12})$, N, $N(R^{10})$, O, with the still further proviso that no more than three of W, one of W, X, Y, and Z is selected from the group consisting optionally and independently selected to be a bond wherein more than one of W, X, Y, and Z is optionally O or S, and of N, N(R10), O, and S, with the further proviso that no W, X, Y, and Z are independently selected from the S and a bond with the proviso that W, X, Y, and Z are K, Y, and Z are optionally N or N(R 10);

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Xº and R¹ or R¹ and R² is optionally bonded together to cycloalkenyl ring having from 5 through 8 members and a form a ring selected from the group consisting of a

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partially saturated heterocyclyl ring having from 5 through substituted with one or more of the group consisting of R*, 8 members, wherein said spacer pair is optionally R10, R11, R12, and R11;

optionally bonded together to form a heterocyclyl ring R2 and R44, R2 and R4b, R2 and R14, or R2 and R15 is having from 5 through 8 members; R2 is optionally a spacer having from 2 through 5 atoms linked to the points of bonding of both R* and R* to form a heterocyclyl ring having from 5 through 8 members;

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from the group consisting of 0, S, C(0), C(S), C(0)0, C(S)0, $OC(0)N(R^{41})$, $(R^{41})NC(0)O$, $SC(S)N(R^{41})$, $(R^{41})NC(S)S$, $SC(O)N(R^{41})$, $\left(\operatorname{CR}^{41}\!R^{42}\right)_q$ wherein q is an integer selected from 1 through 6, independently selected from 0 through 3 and W° is selected C(0)S, C(S)S, $C(O)N(R^{41})$, $(R^{41})NC(O)$, $C(S)N(R^{41})$, $(R^{41})NC(S)$, Z° is selected from the group consisting of a bond, $(R^{41})NC(0)N(R^{42})$, $N(R^{42})C(S)N(R^{41})$, $(R^{41})NC(S)N(R^{42})$, S(0), $(R^{41})NC(0)S$, $OC(S)N(R^{41})$, $(R^{41})NC(S)O$, $N(R^{42})C(O)N(R^{41})$, (CH(R41))g-W0-(CH(R42))p wherein g and p are integers

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 $\text{ON}\left(R^{41}\right)$, and $\text{SiR}^{29}R^{29}$, and $\left(\text{CH}\left(R^{41}\right)\right)_{\bullet}-W^{22}-\left(\text{CH}\left(R^{42}\right)\right)_{h}$ wherein e and $S(0)_{2}$, $S(0)_{2}N(R^{41})$, $N(R^{41})S(0)_{2}$, Se, Se(0), $Se(0)_{2}$, $Se(0)_{2}N(R^{41})$, cyclopropyl, 1,2-cyclobutyl, 1,2-cyclohexyl, 1,3-cyclohexyl, CR''R'3=C; vinylidene), ethynylidene (CGC; 1,2-ethynyl), 1,2h are integers independently selected from 0 through 2 and $N(R^{41})$ Se $\{O\}_2$, P(O) $\{R^9\}$, $N(R^7)$ P(O) $\{R^9\}$, P(O) $\{R^9\}$, $N(R^{41})$, 1,2-cyclopenty1, 1,3-cyclopenty1, 2,3-morpholiny1, 2,4piperidinyl, 3,4-piperidinyl, 1,2-pyrrolidinyl, 1,3-W²² is selected from the group consisting of CR⁴³=CR⁴³, piperazinyl, 2,6-piperazinyl, 1,2-piperidinyl, 1,3morpholinyl, 2,6-morpholinyl, 3,4-morpholinyl, 3,5morpholinyl, 1,2-piperazinyl, 1,3-piperazinyl, 2,3piperidinyl, 2,3-piperidinyl, 2,4-piperidinyl, 2,6-

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tetrahydrofuranyl, wherein W2 is optionally substituted with pyrrolidinyl, 3,4-pyrrolidinyl, 2,3-tetrahydrofuranyl, 2,4tetrahydrofuranyl, 2,5-tetrahydrofuranyl, and 3,4-

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oyrrolidinyl, 2,3-pyrrolidinyl, 2,4-pyrrolidinyl, 2,5-

one or more substituents selected from the group consisting of R^{9} , R^{10} , R^{11} , R^{12} , and R^{11} and with the proviso that Z^{0} is directly bonded to the pyridine ring,

R²⁸ and R²⁹ are independently selected from the group consisting of hydrido, hydroxyalkyl, alkyl, alkenyl, alkynyl, aryl, aralkyl, aryloxyalkyl, acyl, aroyl, aralkanoyl, heteroaroyl, aralkoxyalkyl, alkylsulfinylalkyl, alkylsulfinylalkyl, alkylsulfinylalkyl,

heteroaralkylthioalkyl, alkoxyalkyl, heteroaryloxyalkyl, alkenyloxyalkyl, arylthioalkyl, arylthioalkyl, cycloalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenyl, cycloalkenyl, cycloalkenyl, haloalkenyl, haloalkenyl, haloalkenyl, halocycloalkenyl, haloalkoxyalkyl, haloalkenyloxyalkyl, halocycloalkoxy, halocycloalkoxyalkyl, perhaloaryl, perhaloaryloxyalkyl, heteroaryl, heteroarylalkyl, perhaloarylalkyl, heteroaryl, heteroarylalkyl, heteroaryl, heteroarylalkyl, heteroaryl, heteroarylalkyl,

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halocycloalkenyloxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, heteroaryl, heteroarylalkyl, heteroarylalkyl, heteroarylalkyl, dicyanoalkyl, carboxamidoalkyl, dicarboxamidoalkyl, dicyanocarboalkoxyalkyl, dicyanocycloalkyl, carboxalkoxyalkyl, dicyanocycloalkyl, dicyanocycloalkyl, dicyanocycloalkyl, dicyanocycloalkyl, dicyanocycloalkyl, dicyanocycloalkyl, dicyanocycloalkyl, arboalkoxycycloalkyl, dicarboxloxycycloalkyl, dicyanolycycloalkyl, acylalkyl, arylaulfinylalkyl, arylaulfinyl, cycloalkylsulfinylalkyl, arylaulfinyl, cycloalkylsulfinylylylalkyl, arylaulfinyl, heteroarylaulfonylalkyl, cycloalkyl, heteroarylaulfonylalkyl,

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heteroarylsulfinylalkyl, aralkylsulfinylalkyl, aralkylsulfonylalkyl, carboxy, dialkoxyphosphono, diaralkoxyphosphono, dialkoxyphosphonoalkyl and diaralkoxyphosphonoalkyl;

R²⁸ and R²⁹ are optionally taken together to form a ring selected from the group consisting of a cycloalkyl ring having from 3 through 8 members, a cycloalkenyl ring having from 3 through 8 members, and a heterocyclyl ring having from 3 through 8 members;

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Q is formula (II):

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wherein D^1 , D^2 , J^2 and K^1 are independently selected from the group consisting of C, N, O, S and a bond with the provisos that no more than one can be a bond, no more than one of D^1 , D^2 , J^1 , J^2 and K^1 can be O, no more than one of D^1 , D^2 , J^1 , J^2 and K^1 can be S, one of D^1 , D^2 , J^1 , J^2 and K^1 are O and K^1 must be a bond when two of D^1 , D^2 , J^1 , J^2 and K^1 are O and S^2 , and no more than four of D^1 , D^2 , J^1 , J^2 and K^1 are be N, with the provisos that D^1 , D^2 , J^1 , J^2 and K^1 are selected to maintain an aromatic ring system and that R^2 , R^{19} , R^{19} , and R^{13} are each independently selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen;

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Q is optionally selected from formula (III):

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(III)

wherein D^2 , D^4 , J^3 , and J^4 are independently selected from the group consisting of C, N, O, and S, no more than one of D^3 , J^3 , and J^4 is O, no more than one of D^3 , J^3 , and J^4 is S, and no more than three of D^3 , J^2 , and J^3

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selected to maintain an aromatic ring system and that $extsf{R}^{9},$ nature of nitrogen, the divalent nature of sulfur, and maintain the tetravalent nature of carbon, trivalent are N, with the provisos that D^3 , D^4 , J^3 , and J^4 are R10, R11, and R12 are each independently selected to the divalent nature of oxygen;

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haloalkylthio, alkenyl, alkynyl, saturated heterocyclyl, halocycloalkoxyalkyl, and halocycloalkenyloxyalkyl with Q is optionally selected from the group consisting halocycloalkenyl, haloalkoxyalkyl, haloalkenyloxyalkyl, neteroaroyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, the proviso that Z° is selected from other than a bond of hydrido, alkyl, alkoxy, alkylamino, alkylthio, cycloalkenylalky1, cycloalkylalkenyl, haloalkyl, partially saturated heterocyclyl, acyl, aroyl, haloalkoxy, haloalkenyl, halocycloalkyl, when Q is hydrido;

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K is (CR**R*b), wherein n is an integer selected from L through 4;

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aralkylsulfonylalkyl with the proviso that halo, hydroxy, alkylsulfonylalkyl, haloalkylsulfinyl, arylsulfinylalkyl, R** and R*b are independently selected from the group heteroaralkylthioalkyl, cyanoalkyl, alkylsulfinylalkyl, heteroaryloxyalkyl, alkenyloxyalkyl, alkylthioalkyl, sycloalkylalkyl, haloalkyl, haloalkenyl, heteroaryl, neteroarylsulfinylalkyl, aralkylsulfinylalkyl, and and cyano are bonded to different carbons when nydroxyalkyl, alkyl, alkenyl, aryl, aralkyl, aralkylthioalkyl, arylthioalkyl, cycloalkyl, consisting of halo, hydrido, hydroxy, cyano, arylsulfonylalkyl, heteroarylsulfonylalkyl, aralkoxyalkyl, aryloxyalkyl, alkoxyalkyl, heteroarylalkyl, heteroarylthioalkyl simultaneously present;

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optionally taken together to form a ring selected from R** and R*b, when bonded to the same carbon,

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through 8 members, a cycloalkenyl ring having 5 through 8 members, and a heterocyclyl ring having 5 through 8 the group consisting of a cycloalkyl ring having 3

members;

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 $(R^2)NC(S)S$, $SC(O)N(R^2)$, $(R^2)NC(O)S$, $OC(S)N(R^7)$, $(R^2)NC(S)O$, E' is E', when K is (CR**R*),, wherein E' is selected $C(S)N(R^7)$, $(R^7)NC(S)$, $OC(O)N(R^7)$, $(R^7)NC(O)O$, $SC(S)N(R^7)$, from the group consisting of a bond, O, S, C(O), C(S), $(R^7)NC(S)N(R^8)$, S(O), $S(O)_2$, $S(O)_2N(R^7)$, $N(R^7)S(O)_2$, C(0)0, C(S)0, C(0)S, C(S)S, C(O)N(R7), (R7)NC(O), $S(O)_2N(R^7)C(O)$, $C(O)N(R^7)S(O)_2$, Se, Se(O), $Se(O)_2$, $Se(O)_2N(R^7)$, $N(R^7)Se(O)_2$, $P(O)(R^8)$, $N(R^7)P(O)(R^8)$, $P(O) (R^8) N(R^7)$, $N(R^7)$, $ON(R^7)$, $S1R^{28}R^{29}$, $CR^{4a} = CR^{4b}$, ethynylidene (CmC; 1,2-ethynyl), and CmCR49R4b; $N(R^8)C(O)N(R^7)$, $(R^7)NC(O)N(R^8)$, $N(R^8)C(S)N(R^7)$,

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K is optionally selected to be $(CH(R^{14}))_3$ -T wherein j selected from the group consisting of a bond, 0, S, and $N(R^7)$ with the proviso that $(CH(R^{14}))_j$ is bonded to the is selected from a integer from 0 through 3 and T is

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 E° is optionally $E^{2},$ when K is $\left(CH\left(R^{14}\right)\right)_{3}\text{--}T,$ wherein E^{2} $(R^{2})\,NC(S)\,O,\ N(R^{8})\,C(O)\,N(R^{7})\,,\ (R^{7})\,NC(O)\,N(R^{8})\,,\ N(R^{8})\,C(S)\,N(R^{7})$ C(S)N(R'), (R')NC(S), (R')NC(O)O, (R')NC(S)S, (R')NC(O)S, $S(0)_2N(H)C(0)$, $C(0)N(H)S(0)_2$, Se(0), $Se(0)_2$, $Se(0)_2N(R^7)$, is selected from the group consisting of a bond, C(0), C(S), C(O)O, C(S)O, C(O)S, C(S)S, C(O)N(R⁷), (R⁷)NC(O), $N(R^{2})$ Se $(O)_{2}$, P(O) (R^{0}) , $N(R^{7})$ P(O) (R^{0}) , P(O) (R^{0}) $N(R^{7})$, and $(R^7)NC(S)N(R^9)$, S(0), $S(0)_2$, $S(0)_2N(R^7)$, $N(R^7)S(0)_2$, pyridine ring; N(R');

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selected from the group consisting of 0, S, and $N\left(R^{2}\right)$ with amino, alkylamino, dialkylamino, and sulfhydryl when k is K is optionally selected to be $G^{-}(CH(\mathbb{R}^{15}))_k$ wherein kthe proviso that R15 is other than hydroxy, cyano, halo, is selected from an integer from 1 through 3 and G is

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E⁰ is optionally E¹ when K is G-(CH(R¹⁵))_k wherein E¹ is selected from the group consisting of a bond, O, S, C(O), C(S), C(O)O, C(S)O, C(O)S, C(S)S, C(O)N(R⁷), (R⁷)NC(O), C(S)N(R⁷), (R⁷)NC(O)S, OC(O)N(R⁷), (R⁷)NC(O)O, OC(S)N(R⁷), (R⁷)NC(O)S, OC(S)N(R⁷), (R⁷)NC(O)S, OC(S)N(R⁷), (R⁷)NC(S)O, N(R⁸), (R⁷)NC(S)O, N(R⁸), (R⁸)C(S)N(R⁷), (R⁷)NC(S)O, N(R⁸), S(O), S(O)

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wherein D⁵, D⁶, J⁵, and J⁶ are independently selected from the group consisting of C, N, O, S and a bond with the provisos that no more than one is a bond, K^2 is independently selected from the group consisting of C and N', no more than one of D⁵, D⁶, J⁵, and J⁶ is O, no more than one of D⁵, D⁶, J⁵, and J⁶ is O, no more than one of D⁵, D⁶, J⁶, J⁷, and J⁶ are O and S, no more than three of D⁵, D⁶, J⁵, and J⁶ are N when K⁷ is carbon, with the provisos that R¹⁶, R¹⁷, R¹⁸, and R¹⁸ are each independently selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen and that D⁵, D⁶, J⁵, and J⁶ are selected to maintain an aromatic ring system,

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R¹⁶ and R¹⁷ are independently optionally taken together to form a ring selected from the group consisting of a cycloalkenyl ring having from 5 through 8 members, a partially saturated heterocyclyl ring having from 5 through 8 members, a heteroaryl having from 5 through 6 members, and an aryl;

R¹⁸ and R¹⁹ are independently optionally taken together to form a ring selected from the group consisting of a cycloalkenyl ring having from 5 through 8 members, a partially saturated heterocyclyl ring having from 5 through 8 members, a heteroaryl having from 5 through 6 members, and an aryl;

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Q^b is selected from the group consisting of NR²⁰R²¹, 'NR²⁰R²¹R²², oxy, alkyl, aminoalkyl, alkylamino, dialkylsulfoniumalkyl, acylamino and hydrido, wherein R²⁰, R²¹, and R²² are independently selected from the group consisting of hydrido, amino, alkyl, hydroxy, alkoxy, aminoalkyl, alkylamino, and hydroxyalkyl with the provisos that no more than one of R²⁰, R²¹, and R²² is hydroxy, alkoxy, alkylamino, amino, and dialkylamino at the same time and that R²⁰, R²¹, and R²² must be other than be hydroxy, alkoxy, alkoxy, alkylamino, amino, amino, and dialkylamino when R² is N'; alkoxy, alkylamino, amino, and dialkylamino when R² is N';

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R²⁰ and R²¹, R²⁰ and R²², or R²¹ and R²² is optionally bonded together form a ring having from 4 through 7 atoms connecting the points of bonding of said spacer pair members to form a heterocyclyl ring having 5 through 8 members;

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 Q^b is optionally selected from the group consisting of $N(R^{26}) C(S) SR^{24}$, $N(R^{26}) C(S) SR^{5}$, $N(R^{26}) C(S) SR^{5}$, $N(R^{26}) C(S) SR^{5}$, $N(R^{26}) C(S) SR^{5}$ with the proviso that no more than one of R^{24} , R^{24} , and R^{26} can be hydroxy, alkoxy, aminoalkyl, alkylamino, amino, or dialkylamino when two of the group consisting of R^{24} , R^{24} , and R^{26} are bonded to the same atom,

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 $N(R^{26})C(S)N(R^{23})$ (R^{24}), $C(NR^{25})OR^5$, $C(O)N(R^{26})C(NR^{25})N(R^{23})$ (R^{24}),

 $C(S)N(R^{26})C(NR^{25})N(R^{23})(R^{24})$, $N(R^{26})N(R^{26})C(NR^{25})N(R^{23})(R^{24})$,

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Qb is optionally selected from the group consisting

of dialkylsulfonium, trialkylphosphonium, C(NR25)NR23R24,

 $N(R^{26}) \subset (NR^{25}) N(R^{23}) (R^{24})$, $N(R^{26}) \subset (O) N(R^{23}) (R^{24})$,

haloalkyl, haloalkenyl, halocycloalkyl, halocycloalkenyl, R27 is selected from the group consisting of hydrido, aralkoxyalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, aralkylthioalkyl, heteroaralkylthioalkyl, alkoxyalkyl, heteroaryloxyalkyl, alkenyloxyalkyl, alkylthioalkyl, cycloalkylalkenyl, cycloalkenyl, cycloalkenylalkyl, halocycloalkoxyalkyl, halocycloalkenyloxyalkyl, alkyl, alkenyl, alkynyl, aralkyl, aryloxyalkyl, arylthioalkyl, cycloalkyl, cycloalkylalkyl, haloalkoxyalkyl, haloalkenyloxyalkyl,

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the same atom and that said Qb group is bonded directly to

of the group consisting of R23, R24, and R26 are bonded to

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alkoxy, alkylamino, amino, or dialkylamino when any two

the group consisting of hydrido, alkyl, hydroxy, alkoxy,

aminoalkyl, amino, alkylamino, dialkylamino, and

hydroxyalkyl;

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R23, R24, R25, and R26 are independently selected from

a carbon atom;

that no more than one of \mathbb{R}^{23} , \mathbb{R}^{24} , and \mathbb{R}^{26} can be hydroxy,

C(NR²³)SR⁵, C(O)NR²³R²⁴, and C(O)NR²³R²⁴ with the provisos

 $SN(R^{26}) \subset (NR^{25}) N(R^{23}) (R^{24})$, $N(R^{26}) N(R^{26}) SO_2 N(R^{23}) (R^{24})$,

perhaloaryloxyalkyl, heteroaryl, heteroarylalkyl, heteroarylthioalkyl, heteroaralkylthioalkyl, arylsulfinylalkyl, arylsulfonylalkyl,

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heteroarylsulfonylalkyl, heteroarylsulfinylalkyl, cycloalkylsulfinylalkyl, cycloalkylsufonylalkyl, aralkylsulfinylalkyl and aralkylsulfonylalkyl;

R30 and R31 are independently selected from the group neteroaryloxyalkyl, alkoxy, alkylthio, arylthio, alkyl, consisting of hydrido, hydroxy, thiol, aryloxy, amino, alkenyl, alkynyl; aryl, aralkyl, aryloxyalkyl, alkylamino, dialkylamino, hydroxyalkyl,

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 R^{23} and $R^{25},\ R^{24}$ and $R^{25},\ R^{25}$ and $R^{26},\ and\ R^{23}$

 \mathbb{R}^{23} and \mathbb{R}^{24} are optionally bonded together to form a

heterocyclyl ring having 5 through 8 members;

and R26 are independently optionally selected to form the

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selected from the group consisting of 0, S, C(0), C(S),

group L-U-V wherein L, U, and V are independently

 $\mathbb{C}(J_{H})_{2}$ S(0), SO₂, OP(OR³¹)R³⁰, P(0)R³⁰, P(S)R³⁰, C(R³⁰)R³¹,

 $C=C(R^{10})R^{31}$, (0), POP(0), R^{10} (0) POP(0) R^{30} , Si $(R^{29})R^{28}$,

Si (R²³) R²ªSi (R²³) R²ª, Si (R²³) R²ªOSi (R²³) R²ª, (R³ª) R²ª, (R³²)

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 $(R^{26})\,R^{29}CSC\,(R^{29})\,R^{29}\,,\ C\,(O)\,C\,(R^{30})\,=\!C\,(R^{31})\,\,,\ C\,(S)\,C\,(R^{30})\,=\!C\,(R^{31})\,\,,$

 $OP(OR^{11})R^{10}$, $P(O)R^{10}$, $P(S)R^{10}$, $Si(R^{28})R^{29}$ and $N(R^{10})$, and a

 $P(O) \mathbb{R}^{10} \mathbb{C}(\mathbb{R}^{10}) = \mathbb{C}(\mathbb{R}^{11})$, $P(S) \mathbb{R}^{10} \mathbb{C}(\mathbb{R}^{10}) = \mathbb{C}(\mathbb{R}^{11})$, $D\mathbb{C}(\mathbb{R}^{10})$ $(\mathbb{R}^{11}) \mathbb{D}$,

 $S\left(O\right)\subset\left(\mathbb{R}^{30}\right)=C\left(\mathbb{R}^{31}\right),\quad SO_{2}\subset\left(\mathbb{R}^{30}\right)=C\left(\mathbb{R}^{31}\right),\quad \mathbb{P}\mathbb{R}^{30}\subset\left(\mathbb{R}^{30}\right)=C\left(\mathbb{R}^{31}\right),$

bond with the proviso that no more than any two of L,

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neterocyclyl comprised of by L, U, and V has from 5

through 10 member;

through 2;

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and V are simultaneously covalent bonds and the

aralkylthioalkyl, heteroaralkoxythioalkyl, alkoxyalkyl, aralkoxyalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, heteroaryloxyalkyl, alkenyloxyalkyl, alkylthioalkyl, cycloalkylalkenyl, cycloalkenyl, cycloalkenylalkyl, haloalkyl, haloalkenyl, haloaralkylsulfinylalkyl, arylthioalkyl, cycloalkyl, cycloalkylalkyl,

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aralkylsulfonylalkyl, cyanoalkyl, dicyanoalkyl, cyanocarboalkoxyalkyl, carboalkoxyalkyl, carboxamidoalkyl, dicarboxamidoalkyl, 30

dicarboalkoxyalkyl, cyanocycloalkyl, dicyanocycloalkyl, carboalkoxycyanocycloalkyl, carboalkoxycycloalkyl, dicarboalkoxycycloalkyl, formylalkyl, acylalkyl, carboxamidocycloalkyl, dicarboxamidocycloalkyl,

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D is selected from the group consisting of oxygen, C=O, C=S, S(O) wherein m is an integer selected from 0

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dialkoxyphosphonoalkyl, diaralkoxyphosphonoalkyl, diaralkoxyphosphonoalkoxy, phosphonoalkoxy, phosphonoalkyl, dialkoxyphosphonoalkoxy, dialkoxyphosphonoalkylamino,

S

alkoxysulfonylalkylamino, aralkoxysulfonylalkylamino, and diaralkoxyphosphonoalkylamino, phosphonoalkylamino, dialkoxyphosphonoalkyl, diaralkoxyphosphonoalkyl, aralkoxysulfonylalkyl, alkoxysulfonylalkoxy, aralkoxysulfonylalkoxy, sulfonylalkoxy, sulfonylalkyl, alkoxysulfonylalkyl, oulfonylalkylamino;

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selected from the group consisting of a cycloalkyl ring having from 3 through 8 members, a cycloalkenyl ring having from 3 through 8 members, and a heterocyclyl R30 and R31 are optionally taken to form a ring ring having from 3 through 8 members;

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and \mathbb{R}^{26} is optionally bonded togerther to form the group Lcycloalkyl and cycloalkenyl radicals are substituted with wherein said 1,2-substitutents are independently selected radical, an heteroaryl radical, a saturated heterocyclic from C=O, C=S, C(R²⁸)R¹², S(O), S(O)₂, OP(OR¹¹)R¹⁰, P(O)R¹⁰, R^{23} and $R^{25},\ R^{24}$ and $R^{25},\ R^{25}$ and $R^{26},\ or\ R^{23}$ U-V wherein L, U, and V are independently selected from the group of 1,2-disubstituted radicals consisting of a radical and a partially saturated heterocyclic radical one or more groups selected from R^{10} and R^{11} , an aryl cycloalkyl radical, a cycloalkenyl radical wherein P(S)R30 and S1(R28)R29;

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selected from C=O, C=S, C(\mathbb{R}^{28}) \mathbb{R}^{29} ; S(O), S(O) $_2$, OP(O \mathbb{R}^{31}) \mathbb{R}^{30} , and R26 is optionally bonded together to form the group L- R^{23} and $R^{25},\ R^{24}$ and $R^{25},\ R^{25}$ and $R^{26},\ R^{24}$ and $R^{25},$ or R^{23} radical wherein said 1,2-substitutents are independently U-V wherein L, U, and V are independently selected from the group of radicals consisting of 1,2-disubstituted P(0)R³⁰, P(S)R³⁰, and Si(R²⁸)R²⁹ and said alkylene and alkylene radicals and 1,2-disubstituted alkenylene

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alkenylene radical are substituted with one or more R30 or

R31 substituents;

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C(0)S, C(S)S, $C(0)N(R^{14})$, $(R^{14})NC(0)$, $C(S)N(R^{14})$, $(R^{14})NC(S)$, $(R^{14})NC(S)N(R^{15})$, S(0), $S(0)_2$, $S(0)_2N(R^{14})$, $N(R^{14})S(0)_2$, Se, Q" is selected from the group consisting of a bond, $N(R^7)P(O)(R^8)$, $P(O)(R^8)N(R^7)$, $N(R^{14})$, $ON(R^{14})$, and $SIR^{28}R^{29}$, selected from the group consisting of O, S, C(O), C(S), selected from 1 through 4, and W° is selected from the $(CR^{37}R^{39})_{b}-(W^{0})_{as}$ wherein az is 0 or 1, b is an integer group consisting of O, S, C(O), C(S), C(O)O, C(S)O, (CH(R14), -W1-(CH(R15), wherein c and d are integers independently selected from 1 through 4, and W1 is $N(R^{15})C(O)N(R^{14})$, $(R^{14})NC(O)N(R^{19})$, $N(R^{15})C(S)N(R^{14})$, Se(O), $Se(O)_2$, $Se(O)_2N(R^{17})$, $N(R^{14})Se(O)_2$, $P(O)(R^0)$, $OC(O)N(R^{14})$, $SC(S)N(R^{14})$, $SC(O)N(R^{14})$, $OC(S)N(R^{14})$,

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C(0)0, C(S)0, C(0)S, C(S)S, $C(0)N(R^{14})$, $(R^{14})NC(0)$,

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 $OC(S)N(R^{14})$, $(R^{14})NC(S)O$, $N(R^{15})C(O)N(R^{14})$, $(R^{24})NC(O)N(R^{15})$, $SC(S)N(R^{14})$, $(R^{14})NC(S)S$, $SC(O)N(R^{14})$, $(R^{14})NC(O)S$, $C(S)N(R^{14})$, $(R^{14})NC(S)$, $OC(O)N(R^{14})$, $(R^{14})NC(O)O$,

 $N(R^{15})C(S)N(R^{14})$, $(R^{14})NC(S)N(R^{15})$, S(O), $S(O)_2$, $S(O)_2N(R^{14})$,

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 $N(R^{14}) S(0)_2$, Se, Se(0), Se(0), Se(0), Se(0), $N(R^{14}) Se(0)_2$, integers independently selected from 0 through 2 and \mathtt{w}^{22} $SiR^{29}R^{29}$, and $(CH(R^{14}))_{\bullet}-W^{22}-(CH(R^{15}))_{h}$ wherein e and h are $P(O)(R^{8})$, $N(R^{7})P(O)(R^{8})$, $P(O)(R^{8})N(R^{7})$, $N(R^{14})$, $ON(R^{14})$, is selected from the group consisting of CR"=CR", 25

CR41R42=C; vinylidene), ethynylidene (C=C; 1,2-ethynyl), 1,2-cyclopropyl, 1,2-cyclobutyl, 1,2-cyclohexyl, 1,3cyclohexyl, 1,2-cyclopentyl, 1,3-cyclopentyl, 2,3-

morpholinyl, 2,4-morpholinyl, 2,6-morpholinyl, 3,4piperidinyl, 1,3-piperidinyl, 2,3-piperidinyl, 2,4morpholinyl, 3,5-morpholinyl, 1,2-piperazinyl, 1,3piperidinyl, 2,6-piperidinyl, 3,4-piperidinyl, 1,2piperazinyl, 2,3-piperazinyl, 2,6-piperazinyl, 1,2-30

pyrrolidinyl, 1,3-pyrrolidinyl, 2,3-pyrrolidinyl, 2,4pyrrolidinyl, 2,5-pyrrolidinyl, 3,4-pyrrolidinyl, 2,3tetrahydrofuranyl, 2,4-tetrahydrofuranyl, 2,5-

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tetrahydrofuranyl, and 3,4-tetrahydrofuranyl, with the provisos that $(CR^{17}R^{18})_b$, $(CH(R^{14}))_c$, $(CH(R^{14}))_b$ and are bonded to E';

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through 8 members, and a heterocyclyl ring having from the group consisting of a cycloalkyl ring having from 3 optionally taken together to form a ring selected from through 8 members, a cycloalkenyl ring having from 3 R" and R", when bonded to different carbons, are 3 through 8 members;

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consisting of a cycloalkyl ring having from 3 through 8 nembers, and a heterocyclyl ring having from 3 through taken together to form a ring selected from the group R" and R", when bonded to different carbons, are members, a cycloalkenyl ring having from 3 through 8 nembers;

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nembers, and a heterocyclyl ring having from 3 through 8 consisting of a cycloalkyl ring having from 3 through 8 R³ and R³ , when bonded to different carbons, are taken together to form a ring selected from the group members, a cycloalkenyl ring having from 3 through 8 nembers;

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R" and R", when bonded to the same carbon, are taken together to form a group selected from a group consisting having from 3 through 8 members, and a heterocyclyl ring selected from the group consisting of a cycloalkyl ring having from 3 through 8 members, a cycloalkenyl ring of oxo, thiono, alkylene, haloalkylene, and a ring having from 3 through 8 members;

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 Y^{o} is optionally Y^{AT} wherein $\mathbb{Q}^{\text{b}}\text{-}\mathbb{Q}^{\text{e}};$

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of W' is selected from the group consisting of 0, S, C(0); 1 through 4, and W¹ is selected from the group consisting integer selected from 1 through 6, $(CH(R^{14}))_c-W^1-(CH(R^{15}))_d$ wherein c and d are integers independently selected from c(s), c(o)o, c(s)o, c(o)s, c(s)s, $c(o)N(R^{14})$, $(R^{14})NC(o)$, Y° is optionally Qb-Q" wherein Q" is selected from (CR37 R38), wherein f is an the group consisting of

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integers independently selected from 0 through 2 and W2 is $OC(S)N(R^{14})$, $(R^{14})NC(S)O$, $N(R^{15})C(O)N(R^{14})$, $(R^{14})NC(O)N(R^{15})$, $N(R^{15}) C(S) N(R^{14})$, $(R^{14}) NC(S) N(R^{15})$, S(O), $S(O)_2$, $S(O)_2 N(R^{14})$, $N(R^{14}) S(O)_2$, Se, Se(O), Se(O), Se(O), Se(O), N(R¹⁴) Se(O), $SiR^{29}R^{29}$, and $(CH(R^{14}))_{\bullet}-W^2-(CH(R^{15}))_{h}$ wherein e and h are ethynylidene (CmC; 1,2-ethynyl), and C=CR4R4 with the provisos that $(CR^{17} R^{19})_f$, $(CH(R^{15}))_c$, and $(CH(R^{15}))_a$ are $P(O) (R^8)$, $N(R^7) P(O) (R^8)$, $P(O) (R^8) N(R^7)$, $N(R^{14})$, $ON(R^{14})$, $SC(S)N(R^{14})$, $(R^{14})NC(S)S$, $SC(O)N(R^{14})$, $(R^{14})NC(O)S$, selected from the group consisting of CR "-CR", $C(S)N(R^{14})$, $(R^{14})NC(S)$, $OC(O)N(R^{14})$, $(R^{14})NC(O)O$, bonded to E';

 Y^o is optionally $Q^{b}\!-\!Q^{sss}$ wherein Q^{sss} is $(CH(R^{18}))_r\!-\!W^3$, is an integer selected from 1 through 3, W³ is selected morpholinyl, 2,5-morpholinyl, 2,6-morpholinyl, 3,4morpholinyl, 3,5-morpholinyl, 1,2-piperazinyl, 1,3cyclopentyl, 1,3-cyclopentyl, 2,3-morpholinyl, 2,4from the group consisting of 1,1-cyclopropyl, 1,2cyclopropyl, 1,1-cyclobutyl, 1,2-cyclobutyl, 1,2cyclohexyl, 1,3-cyclohexyl, 1,4-cyclohexyl, 1,2-

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pyrrolidinyl, 2,5-pyrrolidinyl, 3,4-pyrrolidinyl, 2H-2,3pyranyl, 2H-2,4-pyranyl, 2H-2,5-pyranyl, 4H-2,3-pyranyl, 4H-2,4-pyranyl, 4H-2,5-pyranyl, 2H-pyran-2-one-3,4-yl, pyrrolidinyl, 1,3-pyrrolidinyl, 2,3-pyrrolidinyl, 2,4piperidinyl, 3,5-piperidinyl, 3,6-piperidinyl, 1,2piperazinyl, 2,6-piperazinyl, 1,2-piperidinyl, 1,3piperidinyl, 1,4-piperidinyl, 2,3-piperidinyl, 2,4piperidinyl, 2,5-piperidinyl, 2,6-piperidinyl, 3,4piperazinyl, 1,4-piperazinyl, 2,3-piperazinyl, 25

carbon and hyrido containing nitrogen member of the ring tetrahydropyranyl, and 3,5-tetrahydropyranyl, and each 2H-pyran-2-one-4,5-yl, 4H-pyran-4-one-2,3-yl, 2,3tetrahydropyranyl, 2,6-tetrahydropyranyl, 3,4tetrahydrofuranyl, 2,4-tetrahydrofuranyl, 2,5tetrahydropyranyl, 2,4-tetrahydropyranyl, 2,5tetrahydrofuranyl, 3,4-tetrahydrofuranyl, 2,3-

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consisting of R, R10, R11, and R12, with the proviso that optionally substituted with one or more of the group $(CH(R^{16}))_r$ is bonded to B^0 and Q^b is bonded to lowest of the W other than the points of attachment is numbered substituent position of each W^3 ; 28

consisting of R, R10, R11, and R12, with the provisos that carbon and hydrido containing nitrogen member of the ring pyrrolidinyl, 2,5-pyrrolidinyl, 3,4-pyrrolidinyl, 2H-2,3r is an integer selected from 1 through 3, W' is selected pyranyl, 2H-2,4-pyranyl, 2H-2,5-pyranyl, 4H-2,3-pyranyl, Yo is optionally Qb-Q*** wherein Q*** is (CH(R18)),-W*, tetrahydropyranyl, and 3,5-tetrahydropyranyl, and each 4H-2,4-pyranyl, 4H-2,5-pyranyl, 2H-pyran-2-one-3,4-yl, pyrrolidinyl, 1,3-pyrrolidinyl, 2,3-pyrrolidinyl, 2,4optionally substituted with one or more of the group $(CH(\mathbb{R}^{16}))_x$ is bonded to \mathbb{E}^0 and \mathbb{Q}^b is bonded to highest piperazinyl, 2,6-piperazinyl, 1,2-piperidinyl, 1,3piperidinyl, 1,4-piperidinyl, 2,3-piperidinyl, 2,4olperidinyl, 2,5-piperidinyl, 2,6-piperidinyl, 3,4piperidinyl, 3,5-piperidinyl, 3,6-piperidinyl, 1,2cyclopentyl, 1,3-cyclopentyl, 2,3-morpholinyl, 2,4morpholinyl, 2,5-morpholinyl, 2,6-morpholinyl, 3,4morpholinyl, 3,5-morpholinyl, 1,2-piperazinyl, 1,3piperazinyl, 1,4-piperazinyl, 2,3-piperazinyl, 2,5-2H-pyran-2-one-4,5-yl, 4H-pyran-4-one-2,3-yl, 2,3from the group consisting of 1,2-cyclobutyl, 1,2of the W other than the points of attachment is cyclohexyl, 1,3-cyclohexyl, 1,4-cyclohexyl, 1,2cetrahydrofuranyl, 3,4-tetrahydrofuranyl, 2,3cetrahydrofuranyl, 2,4-tetrahydrofuranyl, 2,5cetrahydropyranyl, 2,4-tetrahydropyranyl, 2,5tetrahydropyranyl, 2,6-tetrahydropyranyl, 3,4number substituent position of each W';

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r is an integer selected from 1 through 3, W' is selected Υ^0 is optionally $Q^b\!-\!Q^{\text{ess}}$ wherein Q^{ess} is $(CH(R^{18}))_r\!-\!W^5,$ from the group consisting of 1,4-indenyl, 1,5-indenyl,

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3,4-imidazo(1,2-a)pyridinyl, 3,5-imidazo(1,2-a)pyridinyl, 3,6-imidazo(1,2-a)pyridinyl, 3,7-imidazo(1,2-a)pyridinyl, indenyl, 3,7-indenyl, 2,4-benzofuranyl, 2,5-benzofuranyl, isoindolyl, 1,3-isoindolyl, 3,4-indazolyl, 3,5-indazolyl 2,4-indolyl, 2,5-indolyl, 2,6-indolyl, 2,7-indolyl, 3,4-1,6-indenyl, 1,7-indenyl, 2,7-indenyl, 2,6-indenyl, 2,5benzothiophenyl, 3,7-benzothiophenyl, 2,4-imidazo(1,2imidazo(1,2-a)pyridinyl, 2,7-imidazo(1,2-a)pyridinyl, 2,6-benzofuranyl, 2,7-benzofuranyl, 3,4-benzofuranyl, 3,5-benzofuranyl, 3,6-benzofuranyl, 3,7-benzofuranyl, indolyl, 3,5-indolyl, 3,6-indolyl, 3,7-indolyl, 1,4indenyl, 2,4-indenyl, 3,4-indenyl, 3,5-indenyl, 3,6-3,6-indazolyl, 3,7-indazolyl, 2,4-benzoxazolyl, 2,5isoindolyl, 1,5-isoindolyl, 1,6-isoindolyl, 2,4isoindolyl, 2,5-isoindolyl, 2,6-isoindolyl, 2,7a) pyridinyl, 2,5-imidazo(1,2-a) pyridinyl, 2,6-2,4-benzothiophenyl, 2,5-benzothiophenyl, 2,6benzothiophenyl, 3,5-benzothiophenyl, 3,6penzothiophenyl, 2,7-benzothiophenyl, 3,4-15 10

isoquinolinyl, 4,6-isoquinolinyl, 4,7-isoquinolinyl, 4,8isoquinolinyl, 1,6-isoquinolinyl, 1,7-isoquinolinyl, 1,8isoquinolinyl, 3,4-isoquinolinyl, 3,5-isoquinolinyl, 3,6isoquinolinyl, 3,7-isoquinolinyl, 3,8-isoquinolinyl, 4,5naphthyl, 1,7-naphthyl, 1,8-naphthyl, 2,4-naphthyl, 2,5naphthyl, 2,6-naphthyl, 2,7-naphthyl, 2,8-naphthyl, 2,4benzisoxazolyl, 3,5-benzisoxazolyl, 3,6-benzisoxazolyl, benzoxazolyl, 2,6-benzoxazolyl, 2,7-benzoxazolyl, 3,4-3,7-benzisoxazolyl, 1,4-naphthyl, 1,5-naphthyl, 1,6cinnolinyl, 4,6-cinnolinyl, 4,7-cinnolinyl, and 4,8isoquinolinyl, 3,4-cinnolinyl, 3,5-cinnolinyl, 3,6quinolinyl, 4,8-quinolinyl, 1,4-isoquinolinyl, 1,5quinolinyl, 3,6-quinolinyl, 3,7-quinolinyl, 3,8quinolinyl, 2,5-quinolinyl, 2,6-quinolinyl, 2,7quinolinyl, 2,8-quinolinyl, 3,4-quinolinyl, 3,5quinolinyl, 4,5-quinolinyl, 4,6-quinolinyl, 4,7cinnolinyl, 3,7-cinnolinyl, 3,8-cinnolinyl, 4,5-

cinnolinyl, and each carbon and hydrido containing nitrogen member of the ring of the W⁵ other than the points of attachment is optionally substituted with one or more of the group consisting of R⁵, R¹⁰, R¹¹, and R¹², with the proviso that Q⁵ is bonded to lowest number substituent position of each W⁵ and that (CH(R¹⁸)), is bonded to E⁵;

 Y^o is optionally $Q^b \text{-} Q^{\text{seer}}$ wherein Q^{seer} is $(CH(R^{39}))_z \text{-} W^c,$,4-imidazo(1,2-a)pyridinyl, 3,5-imidazo(1,2-a)pyridinyl, ,6-imidazo(1,2-a)pyridinyl, 3,7-imidazo(1,2-a)pyridinyl, r is an integer selected from 1 through 3, W is selected indenyl, 3,7-indenyl, 2,4-benzofuranyl, 2,5-benzofuranyl, .,6-indenyl, 1,7-indenyl, 2,7-indenyl, 2,6-indenyl, 2,5-,4-indolyl, 2,5-indolyl, 2,6-indolyl, 2,7-indolyl, 3,4oenzothiophenyl, 3,7-benzothiophenyl, 2,4-imidazo(1,2from the group consisting of 1,4-indenyl, 1,5-indenyl, .midazo(1,2-a)pyridinyl, 2,7-imidazo(1,2-a)pyridinyl, lndenyl, 2,4-indenyl, 3,4-indenyl, 3,5-indenyl, 3,6-2,6-benzofuranyl, 2,7-benzofuranyl, 3,4-benzofuranyl, ,5-benzofuranyl, 3,6-benzofuranyl, 3,7-benzofuranyl, ,4-benzothiophenyl, 2,5-benzothiophenyl, 2,6-) pyridinyl, 2,5-imidazo(1,2-a) pyridinyl, 2,6penzothiophenyl, 2,7-benzothiophenyl, 3,4penzothiophenyl, 3,5-benzothiophenyl, 3,6-25 10 15 20

2,4-indolyl, 2,5-indolyl, 2,7-indolyl, 3,4-indolyl, 3,5-indolyl, 3,6-indolyl, 3,7-indolyl, 1,4-isoindolyl, 3,7-indolyl, 1,4-isoindolyl, 1,5-isoindolyl, 1,6-isoindolyl, 2,7-indolyl, 1,5-isoindolyl, 2,6-isoindolyl, 2,7-indazolyl, 3,6-indazolyl, 3,7-indazolyl, 3,4-indazolyl, 3,7-indazolyl, 3,7-indazolyl, 2,7-benzoxazolyl, 3,6-benzoxazolyl, 3,6-benzisoxazolyl, 3,6-benzisoxazolyl, 3,7-benzisoxazolyl, 1,4-naphthyl, 1,5-naphthyl, 1,6-naphthyl, 1,6-naphthyl, 1,6-naphthyl, 2,6-duinolinyl, 2,6-quinolinyl, 2,6-quinolinyl, 2,6-quinolinyl, 2,6-quinolinyl, 2,6-quinolinyl, 3,6-quinolinyl, 3,5-quinolinyl, 3,6-quinolinyl, 3,6-quino

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isoquinolinyl, 4,6-1soquinolinyl, 4,7-1soquinolinyl, 4,8isoquinolinyl, 1,6-isoquinolinyl, 1,7-isoquinolinyl, 1,8isoquinolinyl, 3,4-1soquinolinyl, 3,5-1soquinolinyl, 3,6isoquinolinyl, 3,7-isoquinolinyl, 3,8-isoquinolinyl, 4,5points of attachment is optionally substituted with one or more of the group consisting of $R^9,\ R^{10},\ R^{11},\ and\ R^{12},$ substituent position of each W⁶ and that (CH(R³⁸)), is with the proviso that Q^b is bonded to highest number cinnolinyl, 4,6-cinnolinyl, 4,7-cinnolinyl, and 4,8nitrogen member of the ring of the W other than the quinolinyl, 4,8-quinolinyl, 1,4-isoquinolinyl, 1,5isoquinolinyl, 3,4-cinnolinyl, 3,5-cinnolinyl, 3,6cinnolinyl, and each carbon and hydrido containing cinnolinyl, 3,7-cinnolinyl, 3,8-cinnolinyl, 4,5quinolinyl, 3,6-quinolinyl, 3,7-quinolinyl, 3,8quinolinyl, 4,5-quinolinyl, 4,6-quinolinyl, 4,7bonded to E'.

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In an embodiment of compounds of Formula I or a pharmaceutically acceptable salt thereof,

M is selected from the group consisting of N and N \rightarrow O;

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B is formula (V):
R³⁴

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wherein D^1 , D^2 , J^1 , J^2 and K^1 are independently selected from the group consisting of C, N, O, S and a bond with the provisos that no more than one is a bond, no more than one of D^1 , D^2 , J^1 , J^2 and K^1 is O, no more than one of

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provisos that D^1 , D^2 , J^1 , J^2 and K^1 are selected to maintain be a bond when two of D^1 , D^2 , J^1 , J^2 and K^1 are O and S, and nitrogen, the divalent nature of sulfur, and the divalent an aromatic ring system and that R^{12} , R^{13} , R^{34} , R^{35} , and R^{36} $D^1,\ D^2,\ J^1,\ J^2$ and K^1 is S, one of $D^1,\ D^2,\ J^1,\ J^2$ and K^1 must no more than four of D1, D2, J1, J2 and K1 are N, with the R9, R10, R11, R12, R13, R16, R17, R19, R19, R32, R33, R34, tetravalent nature of carbon, trivalent nature of are each independently selected to maintain the nature of oxygen;

S

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aralkylaryl, aralkyl, aralkenyl, aralkynyl, heterocyclyl, acylalkyl, acylalkoxy, aryloylalkoxy, heterocyclyloxy, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, consisting of heterocyclylalkoxy, N-alkyl-N-arylamino, R15, and R16 are independently selected from the group neterocyclylamino, heterocyclylalkylamino, hydrido, dialkylsulfoniumalkyl, carboxy, heteroaralkylthio, haloalkoxylalkyl, heteroaralkoxy, cycloalkylamino, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, acetamido, haloacetamido, amidino, guanidino, dialkylsulfonium, trialkylphosphonium,

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aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl,

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halocycloalkenyl, cycloalkylsulfinyl,

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heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, halocycloalkenyloxyalkyl, hydroxy, amino, alkoxyamino, thio, nitro, alkylamino, alkylthio, alkylthioalkyl, heteroarylamino-N-alkylamino, heteroaralkylamino, arylamino, aralkylamino, arylthio, arylthioalkyl, cycloalkoxy, cycloalkenyloxy, cycloalkoxyalkyl, cycloalkylsulfonylalkyl, heteroarylamino, Ncycloalkylsulfinylalkyl, cycloalkylsulfonyl, halocycloalkoxyalkyl, halocycloalkenyloxy, cycloalkylalkoxy, cycloalkenyloxyalkyl, arylsulfinylalkyl, arylsulfonylalkyl cycloalkylenedioxy, halocycloalkoxy, 30 32

heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl cycloalkenyl, cycloalkylalkyl, cycloalkenylalkyl, halo, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, aralkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, heteroaryloxy, heteroaryloxyalkyl, heteroarylalkyl, haloalkylenedioxy, cycloalkyl, cycloalkylalkanoyl, heterocyclylsulfonyl, heterocyclylthio, alkanoyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, hydroxyaralkyl, hydroxyalkyl, alkylenylamino, partially saturated heterocyclyl, heteroaryl; arylalkenyl, heteroarylalkenyl, carboxyalkyl, arylsulfinyl, arylsulfonyl, heteroarylthio, alkenyloxy, alkenyloxyalky, alkylenedioxy, arylamidocarbonylamido, carboalkoxyalkyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, monoarylamidosulfonyl, arylsulfonamido, heteroarylsulfinyl, heteroarylsulfonyl alkylsulfonyl, alkylsulfonylalkyl, 10 15 20

carboalkoxyalkenyl, carboxy, carboaralkoxy, carboxamido, carboalkoxy, alkoxycarboxamido, alkylamidocarbonylamido carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl;

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members, a partially saturated heterocyclyl ring having 5 through 8 members, a heteroaryl ring having 5 through 6 R12 and R13, R13 and R14, R14 and R15, or R15 and R16 is R16, R19, R12, R13, R14, R15, and R16 are independently bonded together to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8 optionally Q';

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members, and an aryl;

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heteroarylsulfinylalkyl, heteroarylsulfonylalkyl,

S

B is optionally selected from the group consisting of hydrido, trialkylsilyl, C2-C8 alkyl, C3-C8 alkylenyl, C3-C8 alkyll, C3-C8 alkyll, C3-C8 alkyll, C3-C8 haloalkyl, and C3-C8 haloalkenyl wherein each member of group B may be optionally substituted at any carbon up to and including 6 atoms from the point of attachment of B to A with one or more of the group consisting of R²², R²³, R²⁴, R²⁴, and of the

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adjacent to the \mathbb{R}^{12} position is optionally substituted with optionally substituted with R^{10} , a ring carbon or nitrogen optionally substituted with R11, a ring carbon or nitrogen carbon at the point of attachment of B to A is optionally the point of attachment is optionally substituted with $exttt{R}^{ extstyle s}$ point of attachment is optionally substituted with \mathbb{R}^{12} , a carbon and nitrogen atoms adjacent to the carbon atom at substituted with oxo provided that no more than one ring or \mathbb{R}^{13} , a ring carbon or nitrogen atom adjacent to the \mathbb{R}^9 B is optionally selected from the group consisting atom adjacent to the R13 position and two atoms from the ring carbon or nitrogen atom three atoms from the point substituted with R13, a ring carbon other than the ring. position and two atoms from the point of attachment is R13, and a ring carbon or nitrogen atom four atoms from saturated heterocyclyl, and C4-C9 partially saturated neterocyclyl, wherein each ring carbon is optionally carbon is substituted by oxo at the same time, ring atom three atoms from the point of attachment and of C3-C15 cycloalkyl, C5-C10 cycloalkenyl, C4-C12 of attachment and adjacent to the R10 position is

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the point of attachment and adjacent to the R^{13} and R^{33} positions is optionally substituted with R^{34} ;

A is selected from the group consisting of a bond, (W¹)_{tr}-(CH(R¹⁵))_{pa} and (CH(R¹⁵))_{pa}-(W³)_{tr} wherein rr is 0 or 1, pa is an integer selected from 0 through 6, and W³ is selected from the group consisting of 0, S, C(O), C(S), C(O)S, C(S)O, C(O)N(R²), C(S)N(R³), (R³)NC(O), (R³)NC(O), (R³)NC(O), P(O) (R³), (R³)N(R³), C(NR³)N(R³), (R³)NC(NR³), (R³)NC(NR³)NC(NR³), with the proviso that no more than one of the group consisting of rr and pa is 0 at the same time;

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R' and R' are independently selected from the group consisting of hydrido, hydroxy, alkyl, acyl, aroyl, heteroaroyl, and alkoxyalkyl;

R¹⁴, R¹⁵, R¹⁵, and R¹⁸ are independently selected from the group consisting of hydrido, hydroxy, halo, cyano, hydroxyalkyl, alkoxy, alkyl, alkoxyalkyl, cycloalkyl, cycloalkyl, cycloalkenylalkyl, haloalkyl, haloalkoxy, haloalkoxyalkyl,

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haloalkenyloxyalkyl, halocycloalkoxy,
halocycloalkoxyalkyl, halocycloalkenyloxyalkyl, carboxy,
carboxyalkyl, carboalkoxy, carboxamide, and
carboxamidoalkyl;

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R¹⁴ and R¹⁸ can be independently selected from the group consisting of acyl, aroyl, and heteroaroyl, wherein R¹⁸ is optionally substituted at from one through three of the ring carbons with a substituent selected from the group consisting of R¹⁸, R¹⁷, R¹⁸, and R¹⁹;

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Ψ is selected from the group consisting of NR⁵, O, C(O), C(S), S, S(O), S(O)_{21,} ON(R⁵), P(O)(R⁸), and CR²⁹R¹⁰; R⁵ is selected from the group consisting of hydrido, hydroxy, amino, alkyl, alkoxy, alkoxyalkyl, haloalkyl, acyl, aroyl, and heteroaroyl;

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R³⁹ and R⁴⁰ are independently selected from the group consisting of hydrido, hydroxy, halo, cyano, hydroxyalkyl, acyl, aroyl, heteroaroyl, acylamido,

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alkoxy, alkyl, alkoxyalkyl, haloalkyl, haloalkoxy, haloalkoxyalkyl, alkylsulfonyl, haloalkylsulfonyl, carboxy, carboxyalkyl, carboalkoxy, carboxamide, and carboxamidoalkyl;

Ja is independently selected from the group consisting of N and C- X° ;

Jb is independently selected from the group

consisting of N and C-R¹; $\label{eq:consisting} J\text{C is independently selected from the group}$

or is independently selected from the group consisting of N and $C-R^2 \imath$

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 R^2 , R^1 , and X° are independently selected from the group consisting of Z° -Q, hydrido, alkyl, alkenyl, and halo;

R¹ and X° are independently optionally selected from the group consisting of amino, aminoalkyl, haloalkyl, haloalkyl, haloalkylthio, amino, alkylamino, aminoalkyl, amidino, guanidino, hydroxy, hydroxyamino, alkoxy, hydroxyalkyl, alkoxyamino, thiol, alkylthio, dialkylsulfonium, trialkylphosphonium,

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dialkylsulfoniumalkyl, heteroarylamino, nitro, arylamino, aralkylamino, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, hvdroxyhaloalkyl, cyano, and phosphono:

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hydroxyhaloalkyl, cyano, and phosphono; $K^o \mbox{ and } R^1 \mbox{ are optionally selected to be } -W=X-Y=Z-$

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wherein -W=X-Y=Z- forms a heteroaryl having 5 or 6 members or an aryl; $R^1 \ and \ R^2 \ are \ optionally \ selected \ to be -W=X-Y=Z- wherein -W=X-Y=Z- forms \ a heteroaryl ring having 5 or 6$

members or an aryl; W, X, Y, and Z are independently selected from the group consisting of $C(R^2)$, $C(R^{12})$, $C(R^{11})$, $C(R^{12})$, N, $N(R^{10})$, O, S and a bond with the proviso that W, X, Y, and Z are optionally and independently selected to be a bond wherein one of W, X, Y, and Z is selected from the group consisting of N, $N(R^{10})$, O, and S, with the further proviso that no more than one of W, X, Y, and Z is

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pyrrolidinyl, 1,3-pyrrolidinyl, 2,3-pyrrolidinyl, 2,4-

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piperidinyl, 2,6-piperidinyl, 3,4-piperidinyl, 1,2-

piperazinyl, 2,3-piperazinyl, 2,6-piperazinyl, 1,2piperidinyl, 1,3-piperidinyl, 2,3-piperidinyl, 2,4-

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pyrrolidinyl, 2,5-pyrrolidinyl, 3,4-pyrrolidinyl, 2,3-

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optionally 0 or S, and with the still further proviso that no more than three of W, X, Y, and Z are optionally N or N(R^{19});

X° and R¹ or R¹ and R² is optionally bonded together to form a ring selected from the group consisting of a cycloalkenyl ring having from 5 through 8 members and a partially saturated heterocyclyl ring having from 5 through 8 members, wherein said spacer pair is optionally substituted with one or more of the group consisting of R³, R¹¹, R¹¹, R¹¹, and R¹¹;

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R' 18 Z°-0;

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independently selected from 0 through 3 and W^{o} is selected $P(O)(R^9)$, $N(R^7)P(O)(R^8)$, $P(O)(R^9)N(R^7)$, $N(R^{41})$, $ON(R^{41})$, and $(CR^{41}R^{42})_q$ wherein q is an integer selected from 1 through $N(R^{42})C(S)N(R^{41})$, $(R^{41})NC(S)N(R^{42})$, S(O), $S(O)_2$, $S(O)_2N(R^{41})$, integers independently selected from 0 through 2 and $W^{2\,2}$ 2° is selected from the group consisting of a bond, $N(\mathbb{R}^{41}) S(0)_2$, Se, Se(0), Se(0)₂, Se(0)₂ $N(\mathbb{R}^{41})$, $N(\mathbb{R}^{41}) Se(0)_2$, $S1R^{29}R^{29}$, and $(CH(R^{41}))_e-W^{22}-(CH(R^{42}))_h$ wherein e and h are CR'1R'2=C; vinylidene), ethynylidene (CmC; 1,2-ethynyl), 6, $(CH(R^{41}))_g-W^0-(CH(R^{42}))_p$ wherein g and p are integers $C(S)O, C(O)S, C(S)S, C(O)N(R^{41}), (R^{41})NC(O), C(S)N(R^{41}),$ 1,2-cyclopropyl, 1,2-cyclobutyl, 1,2-cyclohexyl, 1,3from the group consisting of O, S, C(O), C(S), C(O)O, morpholinyl, 2,4-morpholinyl, 2,6-morpholinyl, 3,4morpholinyl, 3,5-morpholinyl, 1,2-piperazinyl, 1,3cyclohexyl, 1,2-cyclopentyl, 1,3-cyclopentyl, 2,3is selected from the group consisting of CR"=CR", $(R^{41})NC(S)S$, $SC(O)N(R^{41})$, $(R^{41})NC(O)S$, $OC(S)N(R^{41})$, $(R^{41}) \, NC(S)$, $OC(O) \, N(R^{41})$, $(R^{41}) \, NC(O) \, O$, $SC(S) \, N(R^{41})$, (R⁴¹) NC(S)O, N(R⁴²) C(O) N(R⁴¹), (R⁴¹) NC(O) N(R⁴²),

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 R^{13} , and with the proviso that Z^0 is directly bonded to the selected from the group consisting of $R^9,\ R^{10},\ R^{11},\ R^{12},\ and$ tetrahydrofuranyl, and 3,4-tetrahydrofuranyl, wherein W^{22} is optionally substituted with one or more substituents tetrahydrofuranyl, 2,4-tetrahydrofuranyl, 2,5pyridine ring;

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haloalkyl, haloalkenyl, halocycloalkyl, halocycloalkenyl, R' and R' are independently selected from the group aralkyl, aryloxyalkyl, aralkoxyalkylalkoxy, alkoxyalkyl, amino, halo, cyano, aryloxy, hydroxyalkyl, acyl, aroyl, consisting of amidino, hydroxyamino, hydrido, hydroxy, heteroaroyl, heteroaryloxyalkyl, alkoxy, alkyl, aryl, cycloalkylalkenyl, cycloalkenyl, cycloalkenylalkyl, halocycloalkenyloxyalkyl, saturated heterocyclyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, neteroaryloxyalkyl, cycloalkyl, cycloalkylalkyl, partially saturated heterocycly1, heteroary1, nalocycloalkoxy, halocycloalkoxyalkyl,

heteroaralkylthioalkyl, alkylsulfonyl, haloalkylsulfonyl, arylsulfonyl, arylsulfonylalkyl, aralkylsulfonyl, heteroarylsulfonylalkyl, heteroarylsulfonyl, and sycloalkylsulfonyl, cycloalkylsufonylalkyl, heteroaralkyl, heteroarylthioalkyl, aralkylsulfonylalkyl;

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Q is formula (II):

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from the group consisting of C, N, O, S and a bond with wherein $D^1,\ D^2,\ J^1,\ J^2$ and K^1 are independently selected (II

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be a bond when two of D1, D2, J1, J2 and K2 are O and S, and independently selected to maintain the tetravalent nature than one of D1, D2, J1, J2 and K1 is O, no more than one of $D^1,\ D^2,\ J^1,\ J^2$ and K^1 is S, one of $D^1,\ D^2,\ J^1,\ J^2$ and K^1 must no more than four of D1, D2, J1, J2 and K1 are N, with the of carbon, trivalent nature of nitrogen, the divalent the provisos that no more than one is a bond, no more nature of sulfur, and the divalent nature of oxygen; proviso that R9, R10, R11, R12, and R13 are each

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(III)

Q is optionally selected from formula (III):

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wherein \mathbb{D}^3 , \mathbb{D}^4 , \mathbb{J}^3 , and \mathbb{J}^4 are independently selected from the group consisting of C, N, O, and S, no more than one are N, with the proviso that R', R'', R'', R'', and R'' are of D³, D⁴, J³, and J⁴ is O, no more than one of D³, D⁴, J³, and J'is S, and no more than three of $D^1,\ D^2,\ J^1,\ and\ J^2$ each independently selected to maintain the tetravalent divalent nature of sulfur, and the divalent nature of nature of carbon, trivalent nature of nitrogen, the oxygen and that $D^1,\ D^2,\ J^1,\ J^2$ and K^1 are selected to maintain an aromatic ring system;

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haloalkylthio, alkenyl, alkynyl, saturated heterocyclyl, Q is optionally selected from the group consisting heteroaroyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, halocycloalkenyl, haloalkoxyalkyl, haloalkenyloxyalkyl, of hydrido, alkyl, alkoxy, alkylamino, alkylthio, cycloalkenylalkyl, cycloalkylalkenyl, haloalkyl, partially saturated heterocyclyl, acyl, aroyl, haloalkoxy, haloalkenyl, halocycloalkyl,

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K is (CR**R*b), wherein n is an integer selected from 1 through 2,

R⁴ and R⁴ are independently selected from the group consisting of halo, hydrido, hydroxy, cyano, hydroxyalkyl, alkyl, alkenyl, alkoxyalkyl, aralkyl, heteroaralkyl, alkylthioalkyl, haloalkyl, haloalkyl, and cyanoalkyl,

E° is E¹, when K is (CR⁴R⁴), wherein E¹ is selected from the group consisting of a bond, O, S, C(O), C(S), C(O)O, C(S)O, C(O)S, C(S)S, C(O)N(R¹), (R²)NC(O), C(S)N(R²), (R²)NC(S), C(O)N(R²), (R²)NC(O)O, SC(S)N(R²), (R²)NC(S)S, SC(O)N(R²), (R²)NC(O)O, SC(S)N(R²), (R²)NC(S)O, N(R³), (R²)NC(S)N(R³), (R²)NC(S)O, N(R³), (R²)NC(S)N(R²), (R²)NC(S)N(R²), S(O), S(O), S(O), S(O), S(O), S(O), N(R²)S(O), S(O), S(O), S(O), N(R²)S(O), S(O), S(O), N(R²), N(R²)S(O), S(O), S(O)

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from a integer from 0 through 2 and T is selected from a integer from 0 through 2 and T is selected from the group consisting of a bond, O, S, and N(R') with the proviso that (CH(R'*)), is bonded to the pyridine ring;

E° is optionally E², when K is (CH(R¹¹)],-T, wherein E² is selected from the group consisting of a bond, C(O), C(S), C(O)O, C(S)O, C(O)S, C(S)S, C(O)N(R¹), (R²)NC(O), C(S)N(R²), (R²)NC(O)O, (R²)NC(S)S, (R²)NC(O)S, (R²)NC(S)O, N(R³), (R²)NC(O)S, (R²)NC(S)O, N(R³)C(O)N(R²), (R²)NC(S)O, S(O)S, S(O)

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K is optionally G-($CH(R^{15})$)_k wherein k isl or 2 and G is selected from the group consisting of O, S, and $N(R^7)$; E° is optionally E^3 when K is G-($CH(R^{15})$)_k, wherein E^3 is selected from the group consisting of a bond, O, S,

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C(O), C(S), C(O)O, C(S)O, C(O)S, C(S)S, C(O)N(R?),

(R?)NC(O), C(S)N(R?), (R?)NC(S), OC(O)N(R?), (R?)NC(O)O,

SC(S)N(R?), (R?)NC(S)S, SC(O)N(R?), (R?)NC(O)S, OC(S)N(R?),

(R?)NC(S)O, N(R.)C(O)N(R?), (R?)NC(O)N(R.), N(R.)C(S)N(R?),

(R?)NC(S)N(R.), S(O), S(O)2, S(O)2, N(R?), N(R?)S(O)2,

P(O) (R.), N(R?)P(O) (R.), P(O) (R.)N(R?), N(R?), ON(R?),

CR***CR**CR**CR**CR**CR**CR**CR**CR***C

Y° is formula (IV):

(IV)

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wherein D⁵, D⁶, J⁵, and J⁶ are independently selected from the group consisting of C, N, O, S and a bond with the provisos that no more than one is a bond, K² is independently selected from the group consisting of C and N⁷, no more than one of D⁵, D⁶, J⁷, and J⁶ is O, no more than one of D⁵, D⁶, J⁷, and J⁶ is O, no more than one of D⁵, D⁶, J⁵, and J⁶ are O and J⁶ must be a bond when two of D⁵, D⁶, J⁵, and J⁶ are O and S, no more than three of D⁵, D⁶, J⁵, and J⁶ are O and S, no more than four of D⁵, D⁶, J⁵, and J⁶ are N when K² is carbon, with the provisos that R¹⁶, R¹⁷, R¹⁸, and R¹⁸ are each independently selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen and that D⁵, D⁶, J⁵, and J⁶ are selected to maintain an aromatic ring system;

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R¹⁶ and R¹⁷ are optionally independently taken together to form a ring selected from the group consisting of a cycloalkenyl ring having from 5 through 8

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members, a partially saturated heterocyclyl ring having

from 5 through 8 members, a heteroaryl having from 5

through 6 members, and an aryl;

 $Q^{\mathtt{b}}$ is selected from the group consisting of $\mathtt{NR}^{\mathtt{20}}\mathtt{R}^{\mathtt{21}},$

R²³, R²⁴, R²⁵, and R²⁶ are independently selected from the group consisting of hydrido, alkyl, hydroxy, alkoxy, aminoalkyl, alkylamino, dialkylamino, amino, and hydroxyalkyl

connecting the points of bonding to form a heterocyclyl R23 and R24 are optionally taken together to form a linear spacer moiety having from 4 through 7 atoms ring having 5 through 8 members;

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through 1, b is an integer selected from 1 through 4, and $SC(O)N(R^{14})$, $OC(S)N(R^{14})$, $N(R^{15})C(O)N(R^{14})$, $(R^{14})NC(O)N(R^{15})$, $(CR^{17}R^{18})_{b^-}(W^0)_{as}$ wherein as is an integer selected from 0c(s), c(o)o, c(s)o, c(o)s, c(s)s, $c(o)n(R^{14})$, $(R^{14})nC(o)$, Q" is selected from the group consisting of a bond, W° is selected from the group consisting of O, S, C(O), $C(S)N(R^{14})$, $(R^{14})NC(S)$, $OC(O)N(R^{14})$, $SC(S)N(R^{14})$,

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 $N(R^{15})C(S)N(R^{14})$, $(R^{14})NC(S)N(R^{15})$, S(O), $S(O)_3$, $S(O)_2N(R^{14})$, $N(R^{14}) \le (O)_2$, $P(O)(R^6)$, $N(R^7) P(O)(R^8)$, $P(O)(R^6) N(R^7)$, $N(R^{14})$, $ON(R^{14})$, $(CH(R^{14}))_c-W^1-(CH(R^{15}))_d$ wherein c and d are

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alkoxy, alkylamino, amino, and dialkylamino when $K^2\ \text{is}\ N^*;$

R20 and R21, R20 and R22, or R21 and R22 are optionally

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bonded together to form a heterocyclyl ring having 5

chrough 8 members;

dialkylamino, and hydroxyalkyl with the provisos that no

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more than one of \mathbb{R}^{20} , \mathbb{R}^{21} , and \mathbb{R}^{22} is hydroxy, alkoxy,

selected from the group consisting of hydrido, amino,

alkyl, hydroxy, alkoxy, aminoalkyl, alkylamino,

dialkylamino, dialkylsulfoniumalkyl, acylamino. and

NR20R21R22, oxy, alkyl, aminoalkyl, alkylamino,

S

hydrido, wherein $R^{20},\ R^{21},\ and\ R^{22}$ are independently

alkylamino, amino, and dialkylamino at the same time and

that R20, R21, and R22 must be other than be hydroxy,

integers independently selected from 1 through 4, and \mathbf{W}^1 c(s), c(o)o, c(s)o, c(o)s, c(s)s, $c(o)N(R^{14})$, $(R^{14})NC(o)$ is selected from the group consisting of O, S, C(O),

 $SC(S)N(R^{14})$, $(R^{14})NC(S)S$, $SC(O)N(R^{14})$, $(R^{14})NC(O)S$, $C(S)N(R^{14})$, $(R^{14})NC(S)$, $OC(O)N(R^{14})$, $(R^{14})NC(O)O$, 20

> alkylamino, amino, and dialkylamino when two of the group consisting of \mathbb{R}^{23} , \mathbb{R}^{24} , and \mathbb{R}^{26} are bonded to the same atom;

N(R26)C(S)OR5 and N(R26)C(S)SR5 with the proviso that no

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of $N(R^{26}) SO_2N(R^{23}) (R^{24})$, $N(R^{26}) C(0) OR^5$, $N(R^{26}) C(0) SR^5$,

more than one of \mathbb{R}^{23} , \mathbb{R}^{24} , and \mathbb{R}^{26} is hydroxy, alkoxy,

Qb is optionally selected from the group consisting

Q is optionally selected from the group consisting

of dialkylsulfonium, trialkylphosphonium, $C\left(NR^{25}\right)NR^{23}R^{24}$,

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 $N(\mathbb{R}^{26})$ C(S) $N(\mathbb{R}^{23})$ (\mathbb{R}^{24}) , $C(\mathbb{N}\mathbb{R}^{25})$ $O\mathbb{R}^5$, C(O) $N(\mathbb{R}^{26})$ $C(\mathbb{N}\mathbb{R}^{25})$ $N(\mathbb{R}^{23})$ (\mathbb{R}^{24}) ,

 $N(R^{26})C(NR^{25})N(R^{23})(R^{24})$, $N(R^{26})C(O)N(R^{23})(R^{24})$,

 $C(S)\,N(R^{26})\,C(NR^{25})\,N(R^{23})\,\left(R^{24}\right),\ N\left(R^{26}\right)N\left(R^{26}\right)C\left(NR^{25}\right)N\left(R^{23}\right)\left(R^{24}\right),$

 $ON\left(R^{26}\right) C\left(NR^{25}\right) N\left(R^{24}\right) \,, \quad N\left(R^{26}\right) N\left(R^{26}\right) SO_2 N\left(R^{23}\right) \,\left(R^{24}\right) \,,$

the group consisting of R13, R14, and R26 are bonded to the same atom and that said Q^b group is bonded directly to a

carbon atom;

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alkoxy, alkylaminol, amino, or dialkylamino when two of

that no more than one of \mathbb{R}^{23} , \mathbb{R}^{24} , and \mathbb{R}^{26} can be hydroxy,

C(NR²⁵) SR⁵, C(O)NR²³R²⁴, and C(O)NR²³R²⁴ with the provisos

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 $N(R^{15})C(S)N(R^{14})$, $(R^{14})NC(S)N(R^{15})$, S(O), $S(O)_2$, $S(O)_2N(R^{14})$, $N(\mathbb{R}^{14})\,S\,(O)_{\,2},\ P\,(O)\,(\mathbb{R}^9)\,,\ N\,(\mathbb{R}^7)\,P\,(O)\,(\mathbb{R}^9)\,,\ P\,(O)\,(\mathbb{R}^9)\,N\,(\mathbb{R}^7)\,,\ N\,(\mathbb{R}^{14})\,,$ $OC(S)N(R^{14})$, $(R^{14})NC(S)O$, $N(R^{15})C(O)N(R^{14})$, $(R^{14})NC(O)N(R^{15})$, integers independently selected from 0 through 2 and \mathtt{W}^{22} $ON(R^{14})$, and $(CH(R^{14}))_a-W^{22}-(CH(R^{15}))_h$ wherein e and h are is selected from the group consisting of CR*=CR*3, 25

CR''R'=C; vinylidene), ethynylidene (CaC; 1,2-ethynyl), 1,2-cyclopropyl, 1,2-cyclobutyl, 1,2-cyclohexyl, 1,3piperazinyl, 2,3-piperazinyl, 2,6-piperazinyl, 1,2morpholinyl, 2,4-morpholinyl, 2,6-morpholinyl, 3,4morpholinyl, 3,5-morpholinyl, 1,2-piperazinyl, 1,3piperidinyl, 1,3-piperidinyl, 2,3-piperidinyl, 2,4cyclohexyl, 1,2-cyclopentyl, 1,3-cyclopentyl, 2,3-35 30

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piperidinyl, 2,6-piperidinyl, 3,4-piperidinyl, 1,2-pyrrolidinyl, 1,3-pyrrolidinyl, 2,3-pyrrolidinyl, 2,4-pyrrolidinyl, 2,5-pyrrolidinyl, 3,4-pyrrolidinyl, 2,5-tetrahydrofuranyl, 2,7-tetrahydrofuranyl, 2,5-tetrahydrofuranyl, 2,5-tetrahydrofuranyl, and 3,4-tetrahydrofuranyl, with the provisos that (CR¹R¹⁸)_b, (CH(R¹¹))_c, and (CH(R¹⁴))_e are bonded to E⁰;

Yo is optionally YAT wherein YAT is Qb-Qe;

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integers independently selected from 0 through 2 and \mathtt{W}^2 is of W is selected from the group consisting of O, S, C(O), 1 through 4, and W¹ is selected from the group consisting integer selected from 1 through 6, (CH(R14))_c-W1-(CH(R15))_d wherein c and d are integers independently selected from $N(R^{14}) S(O)_2$, $P(O)(R^0)$, $N(R^7) P(O)(R^0)$, $P(O)(R^0) N(R^7)$, $N(R^{14})$, $OC(S)N(R^{14})$, $(R^{14})NC(S)O$, $N(R^{15})C(O)N(R^{14})$, $(R^{14})NC(O)N(R^{15})$, $N(R^{15})C(S)N(R^{14})$, $(R^{14})NC(S)N(R^{15})$, S(O), $S(O)_2$, $S(O)_2N(R^{14})$, C(S), C(O)O, C(S)O, C(O)S, $C(O)N(R^{14})$, $(R^{14})NC(O)$, Y° is optionally Qb-Q" wherein Q" is selected from ON(R14), and (CH(R14)),-W2-(CH(R13)), wherein e and h are ethynylidene (CaC; 1,2-ethynyl), and C=CR4Rtb with the provisos that (CR37 R38), (CH(R34)), and (CH(R34)), are (CR37 R38) t wherein f is an $SC(S)N(R^{14})$, $(R^{14})NC(S)S$, $SC(O)N(R^{14})$, $(R^{14})NC(O)S$, selected from the group consisting of CR**≈CR*^b, $C(S)N(R^{14})$, $(R^{14})NC(S)$, $OC(O)N(R^{14})$, $(R^{14})NC(O)O$, the group consisting of bonded to E';

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y° is optilonally Q°-Q°** wherein Q°** is (CH(R)**),-w², r is an integer selected from 1 through 3, W³ is selected from the group consisting of 1,1-cyclopropyl, 1,2-cyclobutyl, 1,2-cyclobutyl, 1,2-cyclobutyl, 1,2-cyclobutyl, 1,3-cyclohexyl, 1,4-cyclohexyl, 1,3-cyclohexyl, 1,4-cyclohexyl, 1,3-cyclopentyl, 2,3-morpholinyl, 2,6-morpholinyl, 2,5-morpholinyl, 1,2-piperazinyl, 1,3-piperazinyl, 1,4-piperazinyl, 2,3-piperazinyl, 2,6-piperazinyl, 1,2-piperidinyl, 1,3-

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pyrrolidinyl, 2,5-pyrrolidinyl, 3,4-pyrrolidinyl, 2H-2,3-Yo is optionally Qb-Qsss wherein Qsss is (CH(R18)),-W4, pyranyl, 2H-2,4-pyranyl, 2H-2,5-pyranyl, 4H-2,3-pyranyl, carbon and hyrido containing nitrogen member of the ring consisting of R9, R10, R11, and R12, with the proviso that pyrrolidinyl, 1,3-pyrrolidinyl, 2,3-pyrrolidinyl, 2,4tetrahydropyranyl, and 3,5-tetrahydropyranyl, and each 4H-2,4-pyranyl, 4H-2,5-pyranyl, 2H-pyran-2-one-3,4-yl, optionally substituted with one or more of the group piperidinyl, 2,5-piperidinyl, 2,6-piperidinyl, 3,4-(CH(R³)), is bonded to E' and Q' is bonded to lowest piperidinyl, 3,5-piperidinyl, 3,6-piperidinyl, 1,2piperidinyl, 1,4-piperidinyl, 2,3-piperidinyl, 2,4-2H-pyran-2-one-4,5-yl, 4H-pyran-4-one-2,3-yl, 2,3of the W3 other than the points of attachment is tetrahydrofuranyl, 2,4-tetrahydrofuranyl,.2,5tetrahydrofuranyl, 3,4-tetrahydrofuranyl, 2,3tetrahydropyranyl, 2,4-tetrahydropyranyl, 2,5tetrahydropyranyl, 2,6-tetrahydropyranyl, 3,4numbered substituent position of each W3; ហ 20 2 15

r is an integer selected from 1 through 3, W is selected pyrrolidinyl, 2,5-pyrrolidinyl, 3,4-pyrrolidinyl, 2H-2,3pyranyl, 2H-2,4-pyranyl, 2H-2,5-pyranyl, 4H-2,3-pyranyl, pyrrolidinyl, 1,3-pyrrolidinyl, 2,3-pyrrolidinyl, 2,4-4H-2,4-pyranyl, 4H-2,5-pyranyl, 2H-pyran-2-one-3,4-yl, piperidinyl, 2,5-piperidinyl, 2,6-piperidinyl, 3,4cyclopentyl, 1,3-cyclopentyl, 2,3-morpholinyl, 2,4morpholiny1, 2,5-morpholiny1, 2,6-morpholiny1, 3,4morpholinyl, 3,5-morpholinyl, 1,2-piperazinyl, 1,3piperazinyl, 2,6-piperazinyl, 1,2-piperidinyl, 1,3piperidiny1, 1,4-piperidiny1, 2,3-piperidiny1, 2,4piperidinyl, 3,5-piperidinyl, 3,6-piperidinyl, 1,2-2H-pyran-2-one-4,5-yl, 4H-pyran-4-one-2,3-yl, 2,3from the group consisting of 1,2-cyclobutyl, 1,2cyclohexyl, 1,3-cyclohexyl, 1,4-cyclohexyl, 1,2piperazinyl, 1,4-piperazinyl, 2,3-piperazinyl,

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2,7-benzoxazolyl, 3,4-benzisoxazolyl, 3,5-benzisoxazolyl, carbon and hydrido containing nitrogen member of the ring r is an integer selected from 1 through 3, $w^{\rm s}$ is selected indenyl, 3,7-indenyl, 2,4-benzofuranyl, 2,5-benzofuranyl, 2,6-indolyl, 2,7-indolyl, 3,4-indolyl, 3,5-indolyl, 3,6consisting of R, R10, R11, and R12, with the provisos that Y^o is optionally $Q^b \text{-} Q^{\text{ess}}$ wherein Q^{ess} is $(CH(R^{1\theta}))_r \text{-} W^5$, 1,6-indenyl, 1,7-indenyl, 2,7-indenyl, 2,6-indenyl, 2,5ndazolyl, 3,5-indazolyl, 3,6-indazolyl, 3,7-indazolyl, 1,5-naphthyl, 1,6-naphthyl, 1,7-naphthyl, 1,8-naphthyl, 2,4-naphthyl, 2,5-naphthyl, 2,6-naphthyl, 2,7-naphthyl, benzothiophenyl, 3,7-benzothiophenyl, 2,7-imidazo(1,2tetrahydropyranyl, and 3,5-tetrahydropyranyl, and each from the group consisting of 1,4-indenyl, 1,5-indenyl, 3,7-imidazo(1,2-a)pyridinyl, 2,4-indolyl, 2,5-indolyl imidazo(1,2-a)pyridinyl, 3,6-imidazo(1,2-a)pyridinyl, indoly1, 3,7-indoly1, 1,4-isoindoly1, 1,5-isoindoly1, 2,4-benzoxazolyl, 2,5-benzoxazolyl, 2,6-benzoxazolyl, 6-benzisoxazolyl, 3,7-benzisoxazolyl, 1,4-naphthyl, 2,6-benzofuranyl, 2,7-benzofuranyl, 3,4-benzofuranyl, indenyl, 2,4-indenyl, 3,4-indenyl, 3,5-indenyl, 3,6-3,5-benzofuranyl, 3,6-benzofuranyl, 3,7-benzofuranyl, 1,6-isoindolyl, 2,4-isoindolyl, 2,5-isoindolyl, 2,6optionally substituted with one or more of the group $(CH(\mathbb{R}^{36}))_r$ is bonded to E' and Q' is bonded to highest isoindolyl, 2,7-isoindolyl, 1,3-isoindolyl, 3,4of the W4 other than the points of attachment is a) pyridinyl, 3,4-imidazo(1,2-a)pyridinyl, 3,5-2,4-benzothiophenyl, 2,5-benzothiophenyl, 2,6tetrahydropyranyl, 2,6-tetrahydropyranyl, 3,4tetrahydrofuranyl, 3,4-tetrahydrofuranyl, 2,3tetrahydropyranyl, 2,4-tetrahydropyranyl, 2,5tetrahydrofuranyl, 2,4-tetrahydrofuranyl, 2,5benzothiophenyl, 2,7-benzothiophenyl, 3,4benzothiophenyl, 3,5-benzothiophenyl, 3,6number substituent position of each W'; 35 50 25 30 15

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 R^9 , R^{10} , R^{11} , and R^{12} , with the provisos that Q^b is bonded to isoquinolinyl, 3,6-isoquinolinyl, 3,7-isoquinolinyl, 3,8isoquinolinyl, 4,5-isoquinolinyl, 4,6-isoquinolinyl, 4,7- Y^0 is optionally $Q^b - Q^{esss}$ wherein Q^{esss} is $(CH(R^{19}))_r - W^6$, r is an integer selected from 1 through 3, W^{ϵ} is selected indenyl, 3,7-indenyl, 2,4-benzofuranyl, 2,5-benzofuranyl, isoquinolinyl, 1,8-isoquinolinyl, 3,4-isoquinolinyl, 3,5isoquinolinyl, 1,5-isoquinolinyl, 1,6-isoquinolinyl, 1,7-2,6-indoly1, 2,7-indoly1, 3,4-indoly1, 3,5-indoly1, 3,6-.,6-indenyl, 1,7-indenyl, 2,7-indenyl, 2,6-indenyl, 2,5hydrido containing nitrogen member of the ring of the W^{\sharp} substituted with one or more of the group consisting of 3,7-imidazo(1,2-a)pyridinyl, 2,4-indolyl, 2,5-indolyl, isoquinolinyl, 4,8-isoquinolinyl, 3,4-cinnolinyl, 3,5from the group consisting of 1,4-indenyl, 1,5-indenyl, benzothiophenyl, 3,7-benzothiophenyl, 2,7-imidazo(1,2lowest number substituent position of each W^{δ} and that imidazo(1,2-a)pyridinyl, 3,6-imidazo(1,2-a)pyridinyl, 3,5-benzofuranyl, 3,6-benzofuranyl, 3,7-benzofuranyl, 2,6-benzofuranyl, 2,7-benzofuranyl, 3,4-benzofuranyl, indenyl, 2,4-indenyl, 3,4-indenyl, 3,5-indenyl, 3,6cinnolinyl, and 4,8-cinnolinyl, and each carbon and 2,8-naphthyl, 2,4-quinolinyl, 2,5-quinolinyl, 2,6other than the points of attachment is optionally cinnolinyl, 3,6-cinnolinyl, 3,7-cinnolinyl, 3,8quinolinyl, 2,7-quinolinyl, 2,8-quinolinyl, 3,4quinolinyl, 3,5-quinolinyl, 3,6-quinolinyl, 3,7quinolinyl, 4,7-quinolinyl, 4,8-quinolinyl, 1,4cinnolinyl, 4,5-cinnolinyl, 4,6-cinnolinyl, 4,7quinoliny1, 3,8-quinoliny1, 4,5-quinoliny1, 4,6-2,4-benzothiophenyl, 2,5-benzothiophenyl, 2,6a) pyridinyl, 3,4-imidazo(1,2-a) pyridinyl, 3,5benzothiophenyl, 2,7-benzothiophenyl, 3,4benzothiophenyl, 3,5-benzothiophenyl, 3,6-(CH(R38)), is bonded to E'; 32 20 25 30 ഗ 10 15

indolyl, 3,7-indolyl, 1,4-isoindolyl, 1,5-isoindolyl,

1,6-isoindolyl, 2,4-isoindolyl, 2,5-isoindolyl, 2,6-

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 R^9 , R^{10} , R^{11} , and R^{12} , with the provisos that Q^9 is bonded to 1,5-isoquinolinyl, 1,5-isoquinolinyl, 1,6-isoquinolinyl, 1,7laoquinolinyl, 4,5-isoquinolinyl, 4,6-isoquinolinyl, 4,7-In another embodiment of compounds of Formula I or a .soquinolinyl, 3,6-isoquinolinyl, 3,7-isoquinolinyl, 3,8-!soquinolinyl, 1,8-isoquinolinyl, 3,4-isoquinolinyl, 3,5- 2,7-benzoxazolyl, 3,4-benzisoxazolyl, 3,5-benzisoxazolyl, hydrido containing nitrogen member of the ring of the W⁶ substituted with one or more of the group consisting of nighest number substituent position of each W⁶ and that indazolyl, 3,5-indazolyl, 3,6-indazolyl, 3,7-indazolyl, ,5-naphthyl, 1,6-naphthyl, 1,7-naphthyl, 1,8-naphthyl, 2,4-naphthyl, 2,5-naphthyl, 2,6-naphthyl, 2,7-naphthyl laoquinolinyl, 4,8-isoquinolinyl, 3,4-cinnolinyl, 3,5-2,4-benzoxazolyl, 2,5-benzoxazolyl, 2,6-benzoxazolyl, 6-benzisoxazolyl, 3,7-benzisoxazolyl, 1,4-naphthyl, cinnolinyl, and 4,8-cinnolinyl, and each carbon and 2,8-naphthyl, 2,4-quinolinyl, 2,5-quinolinyl, 2,6other than the points of attachment is optionally quinolinyl, 2,7-quinolinyl, 2,8-quinolinyl, 3,4quinoliny1, 3,5-quinoliny1, 3,6-quinoliny1, 3,7quinolinyl, 3,8-quinolinyl, 4,5-quinolinyl, 4,6cinnolinyl, 4,5-cinnolinyl, 4,6-cinnolinyl, 4,7quinolinyl, 4,7-quinolinyl, 4,8-quinolinyl, 1,4cinnolinyl, 3,6-cinnolinyl, 3,7-cinnolinyl, 3,8isoindolyl, 2,7-isoindolyl, 1,3-isoindolyl, 3,4-(CH(R38)), is bonded to E0.

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pharmaceutically acceptable salt thereof,

M is selected from the group consisting of N and
N→O;

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B is formula (V):

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wherein D¹, D², J¹, J² and K¹ are independently selected from the group consisting of C, N, O, S and a bond with the provisos that no more than one is a bond, no more than one of D¹, D², J³, J² and K¹ is O, no more than one of D¹, D², J³, J² and K¹ is S, one of D¹, D², J³, J³ and K¹ are O and S, and no more than four of D¹, D², J³, J³ and K¹ are O and S, and no more than four of D¹, D², J³, J³ and K¹ are N, with the provisos that D¹, D², J³, J² and K¹ are selected to maintain an aromatic ring system and that R³; R³², R³², R³³, and R³⁵ are each independently selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen;

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R°, R¹°, R¹¹, R¹², R¹¹, R¹², R¹¹, R¹², R¹³, R¹³, R¹³, R¹¹, R³¹, R³¹, R³¹, and R³² are independently selected from the group consisting of heterocyclylalkoxy, N-alkyl-N-arylamino, heterocyclylalkoylandino, hydrido, acetamido, haloacetamido, amidino, guanidino, dialkylsulfonium, trialkylphosphonium, dialkylsulfoniumalkyl, carboxy, heteroaralkylthio, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, heteroaralkoxy, cycloalkylamino, acylalkyl, acylalkoxy, aryloylalkoxy, heterocyclyloxy, aralkylaryl, aralkylsulfonyl, aralkylsulfonylalkyl, aralkylsulfonyl, aralkylsulfonylalkyl, aralkylsulfonylalkyl, aralkylsulfinyl, halocycloalkyl, aralkylsulfinyl, halocycloalkyl, aralkylsulfinyl, halocycloalkyl,

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carboalkoxyalkenyl, carboxy, carboaralkoxy, carboxamido,

arylamidocarbonylamido, carboalkoxyalkyl,

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carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono,

phosphonoalkyl, diaralkoxyphosphono, and

diaralkoxyphosphonoalkyl;

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optionally Q';

Ris, Rig, Riz, Ril, Rit, Ris, and Ris are independently

heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, halocycloalkenyloxyalkyl, hydroxy, amino, alkoxyamino, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, thio, nitro, alkylamino, alkylthio, alkylthioalkyl, heterocyclylsulfonyl, heterocyclylthio, alkanoyl, arylamino, aralkylamino, arylthio, arylthioalkyl, heteroarylamino-N-alkylamino, heteroaralkylamino, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, cycloalkoxy, cycloalkenyloxy, cycloalkoxyalkyl, cycloalkylsulfinylalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, heteroarylamino, Narylsulfinyl, arylsulfonyl, heteroarylthio, halocycloalkoxyalkyl, halocycloalkenyloxy, heteroarylsulfinyl, heteroarylsulfonyl, monoarylamidosulfonyl, arylsulfonamido, cycloalkylalkoxy, cycloalkenyloxyalkyl, arylsulfinylalkyl, arylsulfonylalkyl, halocycloalkenyl, cycloalkylsulfinyl, cycloalkylenedioxy, halocycloalkoxy, alkylsulfonyl, alkylsulfonylalkyl,

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from the point of attachment and adjacent to the R^{11} and R^{33} atoms from the point of attachment and adjacent to the $R^{10}\,$ substituted with R° or R13, a ring carbon or nitrogen atom substituted with R12, a ring carbon or nitrogen atom three position is optionally substituted with \mathbb{R}^{11} , a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R'2 position is optionally substituted optionally substituted with R³³, a ring carbon other than B is optionally selected from the group consisting C3-C8 alkenyl, C3-C8 alkynyl, C2-C8 haloalkyl, and C3-C8 adjacent to the R' position and two atoms from the point of attachment is optionally substituted with \mathbb{R}^{10} , a ring carbon or nitrogen atom adjacent to the \mathbb{R}^{13} position and of hydrido, trialkylsilyl, C2-C8 alkyl, C3-C8 alkylenyl, haloalkenyl wherein each member of group B is optionally the ring carbon at the point of attachment of B to A is from the point of attachment of B to A with one or more B is optionally selected from the group consisting with R¹³, and a ring carbon or nitrogen atom four atoms than one ring carbon is substituted by oxo at the same substituted at any carbon up to and including 6 atoms optionally substituted with oxo provided that no more time, ring carbon and nitrogen atoms adjacent to the two atoms from the point of attachment is optionally of C3-C12 cycloalkyl, C5-C10 cycloalkenyl, and C4-C9 carbon atom at the point of attachment is optionally saturated heterocyclyl, wherein each ring carbon is of the group consisting of R12, R11, R14, R15, and R16; positions is optionally substituted with R14; 35 20 25 30 15 10

heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl,

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alkenoyl, aroyl, heteroaroyl, aralkanoyl,

cycloalkenyl, cycloalkylalkyl, cycloalkenylalkyl, halo,

haloalkylenedioxy, cycloalkyl, cycloalkylalkanoyl,

alkenyloxy, alkenyloxyalky, alkylenedioxy,

haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl,

carboalkoxy, alkoxycarboxamido, alkylamidocarbonylamido,

heteroaryloxy, heteroaryloxyalkyl, heteroarylalkyl,

arylalkenyl, heteroarylalkenyl, carboxyalkyl,

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partially saturated heterocyclyl, heteroaryl,

aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl,

hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, aralkyl,

hydroxyaralkyl, hydroxyalkyl, alkylenylamino,

A is selected from the group consisting of a bond, $(W^2)_{rr}-(CH(R^{15}))_{pa}$ and $(CH(R^{15}))_{pa}-(W^7)_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 6, and W^7 is selected from the group consisting of 0, S, C(0), C(0) $W(R^7)$, C(S) $W(R^7)$, (R^7)W(C), (R^7)W(C), and $W(R^7)$ with the proviso that no more than one of the group consisting of rr and pa can be 0 at the same time,

R' and R' are independently selected from the group consisting of hydrido, hydroxy, alkyl, and alkoxyalkyl;

 R^{14} , R^{15} , R^{37} , and R^{38} are independently selected from the group consisting of hydrido, hydroxy, halo, alkyl, alkxyalkyl, haloalkyl, haloalkoxy, and haloalkxyalkyl;

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R¹⁴ and R³⁸ are optionally and independently selected from the group consisting of aroyl and heteroaroyl heteroaroyl, wherein R³⁹ is optionally substituted at from one through three of the ring carbons with a substituent selected from the group consisting of R¹⁶, R¹⁷, R¹⁹, and R¹⁹;

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 Ψ is selected from the group consisting of NR5, C(0), and S(0),;

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R⁵ is selected from the group consisting of hydrido, hydroxy, alkyl, and alkoxy;

R¹⁹ and R⁴⁰ are independently selected from the group consisting of hydrido, hydroxy, halo, hydroxyalkyl, alkyl, alkoxyalkyl, haloalkoxy, and haloalkoxyalkyl,

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Ja is independently selected from the group consisting of N and C- X° ;

Jb is independently selected from the group

consisting of N and C-R¹, $\ensuremath{\mathsf{Jc}}$ is independently selected from the group

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consisting of N and C-R2;

X° and R¹ are independently selected from the group consisting of hydrido, alkyl, alkenyl, cyano, halo, haloalkyl, haloalkoxy, haloalkylthio, amino, aminoalkyl,

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alkylamino, amidino, hydroxy, hydroxyamino, alkoxy, hydroxyalkyl, alkoxyamino, thiol, and alkylthio; X° and R¹ or R¹ and R² is optionally -W=X-Y=Zwherein -W=X-Y=Z- forms an aryl or C5-C6 heteroaryl;

W, X, Y, and Z are independently selected from the group consisting of $C(R^{19})$, $C(R^{19})$, $C(R^{11})$, $C(R^{13})$, N, $N(R^{19})$, 0, S, and a bond with the proviso that one of W, X, Y, and Z is of or S, with the further proviso that no more than one of W, X, Y, and Z is 0 or S, with the further proviso that no more than one of W, X, Y, and Z is optionally 0 or S, and with the additional proviso that no more than three of W, X, Y, and Z are optionally N or $N(R^{19})$;

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X° and R¹ or R¹ and R² is optionally bonded together to form C5-C8 cycloalkenyl ring or a partially saturated C5-C8 heterocyclyl ring, wherein said cycloalkenyl ring or heterocyclyl ring is optionally substituted with one or more of the group consisting of R², R¹º, R¹¹, R¹¹, and

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R2 is Z0-Q;

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independently selected from 0 through 3 and W° is selected CR"=CR", 1,2-cyclopropyl, 1,2-cyclobutyl, 1,2-cyclohexyl, and h are integers independently selected from 0 through $(CR^{4,2}R^{4,2})_q$ wherein q is an integer selected from 1 through $N\left(R^{41}\right)$, and $ON\left(R^{41}\right)$, and $\left(CH\left(R^{41}\right)\right)_{\phi}-W^{22}-\left(CH\left(R^{42}\right)\right)_{h}$ wherein e2° is selected from the group consisting of a bond, pyrrolidinyl, 1,3-pyrrolidinyl, 2,3-pyrrolidinyl, 2,4pyrrolidinyl, 2,5-pyrrolidinyl, 3,4-pyrrolidinyl, 2,3-1,3-cyclohexyl, 1,2-cyclopentyl, 1,3-cyclopentyl, 2,3-3, $(CH(R^{41}))_g-W^0-(CH(R^{42}))_p$ wherein g and p are integers from the group consisting of O, S, C(O), S(O), S(O), morpholinyl, 2,4-morpholinyl, 2,6-morpholinyl, 3,4piperidinyl, 1,3-piperidinyl, 2,3-piperidinyl, 2,4piperidinyl, 2,6-piperidinyl, 3,4-piperidinyl, 1,2morpholiny1, 3,5-morpholiny1, 1,2-piperaziny1, 1,3piperazinyl, 2,3-piperazinyl, 2,6-piperazinyl, 1,2-2 and W22 is selected from the group consisting of

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 R^{13} , and with the proviso that Z^0 is directly bonded to the selected from the group consisting of R³, R¹0, R¹1, R¹1, and tetrahydrofuranyl, and 3,4-tetrahydrofuranyl, wherein \mathtt{W}^{22} is optionally substituted with one or more substituents tetrahydrofuranyl, 2,4-tetrahydrofuranyl, 2,5pyridine ring;

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R'1 and R'2 are independently selected from the group consisting of amidino, hydroxyamino, hydrido, hydroxy, amino, and alkyl;

Q is selected from the group consisting of hydrido, with the proviso that Z° is other than a covalent single bond, the formula (II):

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wherein D1, D2, J1, J2 and K1 are independently

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is 0, no more than one of $\mathbb{D}^1,\ \mathbb{D}^2,\ \mathbb{J}^1,\ \mathbb{J}^2$ and K^1 is S, one of independently selected to maintain the tetravalent nature D^1 , D^2 , J^3 , J^2 and K^2 are O and S, and no more than four of covalent bond, no more than one of $D^1,\ D^2,\ J^1,\ J^2$ and K^1 covalent bond with the provisos that no more than one is D^2 , D^2 , J^3 , J^2 and K^1 must be a covalent bond when two of D^2 , J^3 , J^2 and K^1 is N, with the provisos that D^1 , D^2 , selected from the group consisting of C, N, O, S and a J1, J2 and K2 are selected to maintain an aromatic ring of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen; system and that R, R10, R11, R12, and R13 are each K is (CR**R*b), wherein n is 1 or 2;

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R4 and R4b are independently selected from the group consisting of halo, hydrido, hydroxyalkyl, alkyl, alkoxyalkyl, alkylthioalkyl, and haloalkyl,

E° is selected from the group consisting of a bond, C(0), C(S), C(O)N(R²), (R²)NC(O), S(O)₂, (R²)NS(O)₂, and S(O)2N(R7);

Y° is formula (IV):

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provisos that no more than one is a bond, K2 is C, no more oxygen and that $D^5,\ D^6,\ J^5,$ and J^6 are selected to maintain wherein D^{s} , D^{s} , J^{s} , and J^{s} are independently selected from $D^{s},~D^{s},~J^{s},~and~J^{s}$ is S, one of $D^{s},~D^{s},~J^{s},~and~J^{s}$ must be a than one of D^5 , D^6 , J^5 , and J^6 is 0, no more than one of each independently selected to maintain the tetravalent the group consisting of C, N, O, S and a bond with the carbon, with the provisos that R16, R17, R18, and R19 are bond when two of D', D', J', and J' are O and S, and no divalent nature of sulfur, and the divalent nature of more than four of D³, D6, J³, and J6 are N when K² is nature of carbon, trivalent nature of nitrogen, the an aromatic ring system;

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 $NR^{20}R^{21}R^{22}$, aminoalkyl, and hydrido, wherein R^{20} , R^{21} , and R^{23} hydrido, alkyl, hydroxy, amino, aminoalkyl, dialkylamino, are independently selected from the group consisting of Q^{\flat} is selected from the group consisting of $NR^{20}R^{21},$ nore than one of \mathbb{R}^{20} and \mathbb{R}^{21} is selected from the groujp alkylamino, and hydroxyalkyl with the proviso that no

consisting of hydroxy, amino, alkylamino, and dialkylamino at the same time,

Q^b is optionally selected from the group consisting of $C(NR^{25})NR^{23}R^{24}$, $N(R^{26})C(NR^{25})N(R^{24})$, $C(O)N(R^{26})C(NR^{25})N(R^{24})$, $N(R^{26})C(NR^{25})N(R^{25})$, $N(R^{26})C(NR^{25})N(R^{25})N(R^{25})$, $N(R^{26})C(NR^{25})N(R^{25})N(R^{25})$, $N(R^{26})C(NR^{25})N(R^{25})N(R^{25})N(R^{25})$, $N(R^{26})C(NR^{25})N(R^{25})N(R^{25})N(R^{25})$, $N(R^{26})C(NR^{25})N(R^{25})N(R^{25})N(R^{25})$, $N(R^{26})C(NR^{25})N(R^{25})N(R^{25})N(R^{25})N(R^{25})$, $N(R^{26})C(NR^{25})N(R^{25})N(R^{25})N(R^{25})N(R^{25})N(R^{25})N(R^{25})$, $N(R^{26})C(NR^{25})N(R^{25}$

S

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R²¹, R²⁴, R²⁵, and R²⁶ are independently selected from the group consisting of hydrido, alkyl, hydroxy, amino, aminoaminoalkyl, dialkylamino, alkylamino, and hydroxyalkyl;

 $(R^{14})NC(0)$, $C(S)N(R^{14})$, $(R^{14})NC(S)$, $OC(O)N(R^{14})$, $(R^{14})NC(O)O$, and d are integers independently selected from 1 through $OC(S)N(R^{14})$, $(R^{14})NC(S)O$, $N(R^{15})C(O)N(R^{14})$, $(R^{14})NC(O)N(R^{15})$, $N(R^{15}) C(S) N(R^{14})$, $(R^{14}) NC(S) N(R^{15})$, S(0), $S(0)_2$, $S(0)_2 N(R^{14})$, $N(R^{14}) S(0)_2$, $P(0) (R^8)$, $N(R^7) P(0) (R^8)$, $P(0) (R^8) N(R^7)$, $N(R^{14})$, Q is selected from the group consisting of a bond, integers independently selected from 0 through 2 and \mathtt{w}^{22} $N(R^{14}) S(0)_2$, and $N(R^{14})$, $(CH(R^{14}))_c - W^1 - (CH(R^{15}))_d$ wherein c 4 and W^1 is selected from the group consisting of $O,\ S,$ ON(R14), and (CH(R14)),- W^{22} -(CH(R15)), wherein e and h are selected from 1 through 5, and W° is selected from the CR⁴¹R⁴²=C; vinylidene), ethynylidene (CEC; 1,2-ethynyl), .,2-cyclopropyl, 1,2-cyclobutyl, 1,2-cyclohexyl, 1,3-(CR37R38) b- (W0) as wherein az is 0 or 1, b is an integer group consisting of O, C(O), S(O), S(O), S(O), S(O), S(O), N(R14), norpholinyl, 2,4-morpholinyl, 2,6-morpholinyl, 3,4morpholinyl, 3,5-morpholinyl, 1,2-piperazinyl, 1,3piperazinyl, 2,3-piperazinyl, 2,6-piperazinyl, 1,2piperidinyl, 1,3-piperidinyl, 2,3-piperidinyl, 2,4-C(0), C(S), C(0)0, C(S)0, C(0)S, C(S)S, $C(O)N(R^{14})$, syclohexyl, 1,2-cyclopentyl, 1,3-cyclopentyl, 2,3is selected from the group consisting of CR42=CR43 $SC(S)N(R^{14})$, $(R^{14})NC(S)S$, $SC(O)N(R^{14})$, $(R^{14})NC(O)S$,

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piperidinyl, 2,6-piperidinyl, 3,4-piperidinyl, 1,2pyrrolidinyl, 1,3-pyrrolidinyl, 2,3-pyrrolidinyl, 2,4pyrrolidinyl, 2,5-pyrrolidinyl, 3,4-pyrrolidinyl, 2,3tetrahydrofuranyl, 2,4-tetrahydrofuranyl, 2,5tetrahydrofuranyl, and 3,4-tetrahydrofuranyl, with the provisos that (CR¹⁷R²), (CH(R¹⁴)), and (CH(R¹⁴)), are bonded to E°;

Y° is optionally YAT wherein YAT is Qb-Q";

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Y° is optionally Qb-Q** wherein Q** is selected from the group consisting of (CR3' R**), wherein f is an integer selected from 1 through 4, (CH(R**)), c** (CH(R**)), description c and d are integers independently selected from 1 through 2, and W* is selected from the group consisting of 0, S, C(0), C(0) N(R**), (R***)NC(0), N(R***), (R***)NC(0)N(R***), N(R***), (R***)NC(0)N(R***), N(R***), oN(R***), and (CH(R***)), -W**-(CH(R***)), wherein e and h are integers independently selected from 0 through 2 and W* is selected from the group consisting of CR**=CR**, ethynylidene (C%C; 1,2-ethynyl), and C°CR**R** with the provisos that (CR3' R**), (CH(R***)), and (CH(R***)), are bonded to B°;

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y° is optionally Q°-Q*** wherein Q*** is (CH(R)**),-W*, is an integer selected from 1 through 2, W³ is selected from the group consisting of 1,1-cyclobutyl, 1,2-cyclobutyl, 1,2-cyclobutyl, 1,2-cyclobutyl, 1,3-cyclobexyl, 1,4-cyclobutyl, 1,2-cyclobexyl, 1,3-morpholinyl, 2,4-morpholinyl, 2,5-morpholinyl, 2,6-morpholinyl, 2,5-piperazinyl, 1,4-piperazinyl, 1,2-piperazinyl, 1,3-piperazinyl, 1,4-piperazinyl, 1,2-piperidinyl, 2,5-piperidinyl, 2,5-piperidinyl, 2,5-piperidinyl, 2,5-piperidinyl, 2,5-piperidinyl, 3,5-piperidinyl, 3,6-piperidinyl, 3,5-piperidinyl, 3,6-piperidinyl, 1,2-morpholidyl, 3,6-piperidinyl, 1,2-morpholidyl, 3,6-piperidinyl, 1,2-morpholidyl, 3,6-piperidinyl, 1,2-morpholidyl, 1,3-morpholidyl, 1,3-morp

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piperidinyl, 3,5-piperidinyl, 3,6-piperidinyl, 1,2pyrrolidinyl, 1,3-pyrrolidinyl, 2,3-pyrrolidinyl, 2,4pyrrolidinyl, 2,5-pyrrolidinyl, 3,4-pyrrolidinyl, 2H-2,3-

pyrrolidinyl, 2,5-pyrrolidinyl, 3,4-pyrrolidinyl, 2H-2,3r is an integer selected from 1 through 2, W* is selected carbon and hyrido containing nitrogen member of the ring Y^0 is optionally $Q^b\!-\!Q^{\text{eer}}$ wherein Q^{eer} is $\left(CH\left(R^{18}\right)\right)_r\!-\!W^4,$ pyranyl, 2H-2,4-pyranyl, 2H-2,5-pyranyl, 4H-2,3-pyranyl, consisting of R, R10, R11, and R12, with the proviso that pyranyl, 2H-2,4-pyranyl, 2H-2,5-pyranyl, 4H-2,3-pyranyl, pyrrolidinyl, 1,3-pyrrolidinyl, 2,3-pyrrolidinyl, 2,4tetrahydropyranyl, and 3,5-tetrahydropyranyl, and each 4H-2,4-pyranyl, 4H-2,5-pyranyl, 2H-pyran-2-one-3,4-yl, 4H-2,4-pyranyl, 4H-2,5-pyranyl, 2H-pyran-2-one-3,4-yl, optionally substituted with one or more of the group norpholinyl, 3,5-morpholinyl, 1,2-piperazinyl, 1,3piperazinyl, 1,4-piperazinyl, 2,3-piperazinyl, 2,5morpholinyl, 2,5-morpholinyl, 2,6-morpholinyl, 3,4oiperazinyl, 2,6-piperazinyl, 1,2-piperidinyl, 1,3piperidinyl, 1,4-piperidinyl, 2,3-piperidinyl, 2,4- $(CH(\mathbb{R}^{16}))_r$ is bonded to E^0 and \mathbb{Q}^b is bonded to lowest cyclopentyl, 1,3-cyclopentyl, 2,3-morpholinyl, 2,4piperidinyl, 2,5-piperidinyl, 2,6-piperidinyl, 3,4oiperidinyl, 3,5-piperidinyl, 3,6-piperidinyl, 1,2-2H-pyran-2-one-4,5-yl, 4H-pyran-4-one-2,3-yl, 2,3-2H-pyran-2-one-4,5-y1, 4H-pyran-4-one-2,3-y1, 2,3from the group consisting of 1,2-cyclobutyl, 1,2cyclohexyl, 1,3-cyclohexyl, 1,4-cyclohexyl, 1,2of the W³ other than the points of attachment is cetrahydrofuranyl, 3,4-tetrahydrofuranyl, 2,3cetrahydrofuranyl, 2,4-tetrahydrofuranyl, 2,5tetrahydropyranyl, 2,4-tetrahydropyranyl, 2,5tetrahydropyranyl, 2,6-tetrahydropyranyl, 3,4tetrahydrofuranyl, 3,4-tetrahydrofuranyl, 2,3tetrahydrofuranyl, 2,4-tetrahydrofuranyl, 2,5tetrahydropyranyl, 2,4-tetrahydropyranyl, 2,5tetrahydropyranyl, 2,6-tetrahydropyranyl, 3,4numbered substituent position of each \mathtt{W}^3 ;

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consisting of R3, R10, R11, and R12, with the provisos that carbon and hyrido containing nitrogen member of the ring optionally substituted with one or more of the group (CH(R38)), is bonded to Eo and Qb is bonded to highest of the W other than the points of attachment is

number substituent position of each W';

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Y° is optionally Qb-Qsess wherein Qsess is (CH(R38)), - WS, r is an integer selected from 1 through 2, W⁵ is selected 2,7-benzoxazoly1, 3,4-benzisoxazoly1, 3,5-benzisoxazoly1, indenyl, 3,7-indenyl, 2,4-benzofuranyl, 2,5-benzofuranyl, 2,6-indolyl, 2,7-indolyl, 3,4-indolyl, 3,5-indolyl, 3,6-1,6-indenyl, 1,7-indenyl, 2,7-indenyl, 2,6-indenyl, 2,5indazolyl, 3,5-indazolyl, 3,6-indazolyl, 3,7-indazolyl, 1,5-naphthyl, 1,6-naphthyl, 1,7-naphthyl, 1,8-naphthyl, 3,7-imidazo(1,2-a)pyridinyl, 2,4-indolyl, 2,5-indolyl, from the group consisting of 1,4-indenyl, 1,5-indenyl, benzothiophenyl, 3,7-benzothiophenyl, 2,7-imidazo(1,2indolyl, 3,7-indolyl, 1,4-isoindolyl, 1,5-isoindolyl, 3,6-benzisoxazolyl, 3,7-benzisoxazolyl, 1,4-naphthyl; 2,4-benzoxazolyl, 2,5-benzoxazolyl, 2,6-benzoxazolyl, 2,6-benzofuranyl, 2,7-benzofuranyl, 3,4-benzofuranyl, 3,5-benzofuranyl, 3,6-benzofuranyl, 3,7-benzofuranyl, imidazo(1,2-a)pyridinyl, 3,6-imidazo(1,2-a)pyridinyl, 1,6-isoindolyl, 2,4-isoindolyl, 2,5-isoindolyl, 2,6indenyl, 2,4-indenyl, 3,4-indenyl, 3,5-indenyl, 3,6isoindolyl, 2,7-isoindolyl, 1,3-isoindolyl, 3,4-2,4-benzothiophenyl, 2,5-benzothiophenyl, 2,6a) pyridinyl, 3,4-imidazo(1,2-a) pyridinyl, 3,5benzothiophenyl, 2,7-benzothiophenyl, 3,4benzothiophenyl, 3,5-benzothiophenyl, 3,6-

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2,4-naphthyl, 2,5-naphthyl, 2,6-naphthyl, 2,7-naphthyl,

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2,8-naphthyl, 2,4-quinolinyl, 2,5-quinolinyl, 2,6quinolinyl, 2,7-quinolinyl, 2,8-quinolinyl, 3,4quinolinyl, 3,5-quinolinyl, 3,6-quinolinyl, 3,7quinolinyl, 3,8-quinolinyl, 4,5-quinolinyl, 4,6-

quinolinyl, 4,7-quinolinyl, 4,8-quinolinyl, 1,4-

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tetrahydropyranyl, and 3,5-tetrahydropyranyl, and each

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isoquinolinyl, 1,5-isoquinolinyl, 1,6-isoquinolinyl, 1,7-isoquinolinyl, 1,8-isoquinolinyl, 3,4-isoquinolinyl, 3,5-isoquinolinyl, 3,7-isoquinolinyl, 3,6-isoquinolinyl, 3,7-isoquinolinyl, 4,5-isoquinolinyl, 4,6-isoquinolinyl, 4,7-isoquinolinyl, 4,8-isoquinolinyl, 3,4-cinmolinyl, 3,5-cinmolinyl, 3,6-cinmolinyl, 3,7-cinmolinyl, 3,8-cinmolinyl, 4,5-cinmolinyl, 3,7-cinmolinyl, 4,5-cinmolinyl, 4,6-cinmolinyl, 4,7-cinmolinyl, 4,6-cinmolinyl, 4,7-cinmolinyl, and 4,8-cinmolinyl, and each carbon and hyrido containing nitrogen member of the ring of the W⁵ other than the points of attachment is optionally substituted with one or more of the group consisting of R⁵, R¹⁰, R¹¹, and R¹², with the proviso that Q⁵ is bonded to lowest number substituent position of each W⁵ and that (CH(R¹⁸)), is bonded to B⁵,

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Yo is optionally Qb-Q**** wherein Q**** is (CH(R13)), r-W6, r is an integer selected from 1 through 2, W* is selected indenyl, 3,7-indenyl, 2,4-benzofuranyl, 2,5-benzofuranyl, 2,7-benzoxazolyl, 3,4-benzisoxazolyl, 3,5-benzisoxazolyl, ,6-indenyl, 1,7-indenyl, 2,7-indenyl, 2,6-indenyl, 2,5-2,6-indolyl, 2,7-indolyl, 3,4-indolyl, 3,5-indolyl, 3,6indazoly1, 3,5-indazoly1, 3,6-indazoly1, 3,7-indazoly1, from the group consisting of 1,4-indenyl, 1,5-indenyl, penzothiophenyl, 3,7-benzothiophenyl, 2,7-imidazo(1,2-3,7-imidazo(1,2-a)pyridinyl, 2,4-indolyl, 2,5-indolyl, ,6-benzofuranyl, 2,7-benzofuranyl, 3,4-benzofuranyl, 3,5-benzofuranyl, 3,6-benzofuranyl, 3,7-benzofuranyl, imidazo(1,2-a)pyridinyl, 3,6-imidazo(1,2-a)pyridinyl, indolyl, 3,7-indolyl, 1,4-isoindolyl, 1,5-isoindolyl, indenyl, 2,4-indenyl, 3,4-indenyl, 3,5-indenyl, 3,6-.,6-isoindolyl, 2,4-isoindolyl, 2,5-isoindolyl, 2,6-2,4-benzoxazolyl, 2,5-benzoxazolyl, 2,6-benzoxazolyl, lsoindoly1, 2,7-isoindoly1, 1,3-isoindoly1, 3,4-,4-benzothiophenyl, 2,5-benzothiophenyl, 2,6a) pyridinyl, 3,4-imidazo(1,2-a) pyridinyl, 3,5penzothiophenyl, 2,7-benzothiophenyl, 3,4benzothiophenyl, 3,5-benzothiophenyl, 3,6-

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isoquinolinyl, 4,5-isoquinolinyl, 4,6-isoquinolinyl, 4,7-R9, R10, R11, and R12, with the proviso that Qb is bonded to isoquinolinyl, 1,5-isoquinolinyl, 1,6-isoquinolinyl, 1,7isoquinolinyl, 1,8-isoquinolinyl, 3,4-isoquinolinyl, 3,5isoquinolinyl, 3,6-isoquinolinyl, 3,7-isoquinolinyl, 3,8substituted with one or more of the group consisting of hyrido containing nitrogen member of the ring of the W^{ε} highest number substituent position of each W and that 1,5-naphthyl, 1,6-naphthyl, 1,7-naphthyl, 1,8-naphthyl, 2,4-naphthyl, 2,5-naphthyl, 2,6-naphthyl, 2,7-naphthyl, isoquinolinyl, 4,8-isoquinolinyl, 3,4-cinnolinyl, 3,5- S. 6-benzisoxazolyl, 3,7-benzisoxazolyl, 1,4-naphthyl, cinnolinyl, and 4,8-cinnolinyl, and each carbon and 2,8-naphthyl, 2,4-quinolinyl, 2,5-quinolinyl, 2,6other than the points of attachment is optionally quinolinyl, 3,8-quinolinyl, 4,5-quinolinyl, 4,6cinnolinyl, 3,6-cinnolinyl, 3,7-cinnolinyl, 3,8cinnolinyl, 4,5-cinnolinyl, 4,6-cinnolinyl, 4,7quinolinyl, 2,7-quinolinyl, 2,8-quinolinyl, 3,4quinolinyl, 3,5-quinolinyl, 3,6-quinolinyl, 3,7quinolinyl, 4,7-quinolinyl, 4,8-quinolinyl, 1,4-(CH(R38)), is bonded to E0.

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In a preferred embodiment of a compound of Formula I, said compound is the Formula:

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or a pharmaceutically acceptable salt thereof, wherein; M is N or N \rightarrow O;

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B is phenyl or a heteroaryl of 5 or 6 ring members, wherein a nitrogen with a removable hydrogen or a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to A is optionally substituted by R²³, a nitrogen with a removable hydrogen or a carbon

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or a carbon adjacent to \mathbb{R}^{16} and two atoms from the point of at the other position adjacent to the point of attachment substituted by R33, a nitrogen with a removable hydrogen nitrogen with a removable hydrogen or a carbon adjacent removable hydrogen or a carbon adjacent to \mathbb{R}^{12} and two is optionally substituted by R36, a nitrogen with a to both R¹³ and R¹⁵ is optionally substituted by R¹⁴; attachment is optionally substituted by \mathbb{R}^{15} , and a atoms from the point of attachment is optionally

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alkyl, alkenyl, halo, haloalkyl, haloalkenyl, haloalkoxy, alkylsulfonamido, amidosulfonyl, alkanoyl, haloalkanoyl, heteroarylamino, heteroaralkylamino, heterocyclylamino, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, heteroarylsulfonyl, alkylsulfonylalkyl, aryl, aralkyl, cycloalkylsulfinyl, heteroarylsulfinyl, alkylsulfonyl, hydrido, acetamido, haloacetamido, amidino, guanidino, R9, R10, R11, R12, R13, R31, R34, R35, and R36 are haloalkoxyalkyl, carboxyalkyl, carboalkoxy, carboxy, independently selected from the group consisting of arylsulfonyl, aralkylsulfonyl, cycloalkylsulfonyl, heterocyclylalkylamino, alkylthio, alkylthioalkyl, heterocyclylalkoxy, alkoxyalkyl, haloalkoxylalkyl, alkylenedioxy, haloalkylthio, alkanoyloxy, alkoxy, cycloalkoxy, cycloalkylalkoxy, aralkoxy, aryloxy, nydroxy, amino, alkoxyamino, nitro, alkylamino, heteroaryloxy, heteroaralkoxy,heterocyclyloxy, N-alkyl-N-arylamino, arylamino, aralkylamino, alkylsulfinyl, arylsulfinyl, aralkylsulfinyl, hydroxyhaloalkyl, hydroxyalkyl, aminoalkyl, carboxamido, carboxamidoalkyl, and cyano;

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 R^{32} , R^{33} , R^{34} , R^{35} , and R^{36} are independently optionally

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B is optionally selected from the group consisting

wherein each member of group B is optionally substituted

C3-C8 alkenyl, C3-C8 alkynyl, and C2-C8 haloalkyl,

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of hydrido, trialkylsilyl, C2-C8 alkyl, C3-C8 alkylenyl,

at any carbon up to and including 6 atoms from the point of attachment of B to A with one or more of the group consisting of R^{12} , R^{13} , R^{14} , R^{15} , and R^{16} ;

adjacent to the R12 position is optionally substituted with atoms from the point of attachment and adjacent to the \mathtt{R}^{10} position is optionally substituted with \mathbb{R}^{11} , a ring carbon substituted with R' or R11, a ring carbon or nitrogen atom or nitrogen three atoms from the point of attachment and optionally substituted with R¹³, a ring carbon other than time, ring carbons and a nitrogen adjacent to the carbon adjacent to the R' position and two atoms from the point of attachment is optionally substituted with \mathbb{R}^{10} , a ring the ring carbon at the point of attachment of B to A is carbon or nitrogen adjacent to the R13 position and two than one ring carbon is substituted by oxo at the same R13, and a ring carbon or nitrogen four atoms from the optionally substituted with oxo provided that no more substituted with R13, a ring carbon or nitrogen three saturated heterocyclyl, wherein each ring carbon is B is optionally a C3-C12 cycloalkyl or C4-C9 point of attachment and adjacent to the R11 and R11 atoms from the point of attachment is optionally atom at the point of attachment are optionally

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 $(W^7)_{rr}$ - $(CH(R^{15}))_{pa}$, and $(CH(R^{15}))_{pa}$ - $(W^7)_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 6, and W7 is A is selected from the group consisting of a bond, selected from the group consisting of O, S, C(O), positions is optionally substituted with R34;

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more than one of the group consisting of rr and pa is 0 (R')NC(O), (R')NC(S), and N(R') with the proviso that no

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R' is selected from the group consisting of hydrido, hydroxy, and alkyl;

R15 is selected from the group consisting of hydrido, hydroxy, halo, alkyl, and haloalkyl; W is NH or NOH;

Ja is Nor C-X°;

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b is N or C-R1;

X° and R¹ are independently selected from the group consisting of hydrido, alkyl, alkenyl, cyano, halo, haloalkyl, haloalkoxy, haloalkylthio, amino, aminoalkyl, alkylamino, amidino, hydroxy, hydroxyamino, alkoxy, hydroxyalkyl, alkoxyamino, thiol, and alkylthio;

 X^o and R^1 or R^1 and R^2 is optionally -W=X-Y=Z- wherein -W=X-Y=Z- forms an aryl or C5-C6 heteroaryl;

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W, X, Y, and Z are independently selected from the group consisting of $C(R^9)$, $C(R^{10})$, $C(R^{11})$, $C(R^{12})$, N, $N(R^{10})$, O, S, and a bond with the proviso that one of W, X, Y, and Z is 0 or S, with the further proviso that no more than one of W, X, Y, and Z is 0 or S, with the further proviso that no more than one of W, X, Y, and Z is optionally O or S, and with the additional proviso that no more than three of W, X, Y, and Z are optionally N or $N(R^{10})$;

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X° and R¹ or R¹ and R² is optionally bonded together to form C5-C8 cycloalkenyl ring or a partially saturated C5-C8 heterocyclyl ring, wherein said cycloalkenyl ring or heterocyclyl ring is optionally substituted with one or more of the group consisting of R³, R¹¹, R¹¹, and

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R2 is Z0-Q;

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 Z° is selected from the group consisting of a bond, $(CR^{4,1}R^{4})_{\mathfrak{q}}$ wherein q is an integer selected from 1 through 3, and $(CH(R^{4)})_{\mathfrak{g}}-W^{\circ}-(CH(R^{42}))_{\mathfrak{p}}$ wherein g and p are integers independently selected from 0 through 3 and W° is selected from the group consisting of 0, §, C(O), S(O), N(R^{41}), and ON(R^{41});

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Z° is optionally (CH(R'¹))_e-W²-(CH(R'³))_n wherein e and h are independently 0 or 1 and W²¹ is selected from the group consisting of CR'¹-CR'², 1,2-cyclopropyl, 1,2-cyclobexyl, 1,3-cyclohexyl, 1,3-cyclohexyl, 1,3-cyclohexyl, 1,3-morpholinyl, 2,4-morpholinyl, 2,6-morpholinyl, 3,5-

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morpholinyl, 1,2-piperazinyl, 1,3-piperazinyl, 2,3-piperazinyl, 2,6-piperazinyl, 1,2-piperidinyl, 1,3-piperidinyl, 2,3-piperidinyl, 1,2-piperidinyl, 2,6-piperidinyl, 2,4-piperidinyl, 2,6-piperidinyl, 1,2-pyrrolidinyl, 1,3-pyrrolidinyl, 2,3-pyrrolidinyl, 2,5-pyrrolidinyl, 2,3-pyrrolidinyl, 2,5-pyrrolidinyl, 2,5-pyrrolidinyl, 2,5-pyrrolidinyl, 2,5-tetrahydrofuranyl, 2,5-tetrahydrofuranyl, and 3,4-tetrahydrofuranyl, 2,5-tetrahydrofuranyl, and 3,4-tetrahydrofuranyl, wherein 2° is directly bonded to the pyridine ring and W²² is optionally substituted with one or more substituents selected from the group consisting of R², R¹⁰, R¹¹, R¹², and R¹³;

R" and R" are independently selected from the group consisting of amidino, hydroxyamino, hydrido, hydroxy, amino, and alkyl;

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Q is phenyl or a heteroaryl of 5 or 6 ring members, wherein a nitrogen with a removable hydrogen or a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to 2° is optionally substituted by R°, a nitrogen with a removable hydrogen or a carbon at the other position adjacent to the point of attachment is optionally substituted by R¹, a nitrogen with a removable hydrogen or a carbon adjacent to R° and two atoms from the point of attachment is optionally substituted by R¹°, a nitrogen with a removable hydrogen or a carbon adjacent to R¹¹ and two atoms from the point of attachment is optionally substituted by R¹², and a nitrogen with a removable hydrogen or a carbon adjacent to both R¹° and R¹² optionally substituted by R¹²,

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is optionally substituted by \mathbb{R}^{11} ; Q is optionally hydrido with the proviso that \mathbb{Z}^0 is

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K is CR"R";

selected from other than a bond;

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R** and R** are independently selected from the group consisting of halo, hydrido, hydroxyalkyl, alkyl, alkylthioalkyl, and haloalkyl;

 $E^{0},$ with the proviso that K is $CR^{48}R^{4b},$ is $E^{1}wherein\ E^{1}$ is selected from the group consisting of a covalent

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single bond, C(0)N(H), (H)NC(0), C(S)N(H), (H)NC(S),
S(0)₂N(H), N(H)S(0)₂, S(0)₂N(H)C(0), and C(0)N(H)S(0)₂;

K is optionally $(CH(R^{i4}))_3-T$ wherein j is 0 or 1 and T is a bond or $N(R^3)$ with the proviso that $(CH(R^{i4}))_3$ is bonded to the phenyl ring;

S

 R^{14} is selected from the group consisting of hydrido, halo, alkyl, and haloalkyl;

 $E^o,$ with the proviso that K is $(CH(R^{14}))_3\text{-T},$ is E^2 wherein E^2 is selected from the group consisting of $C(O)\,N(H)$, $(H)\,NC(O)$, $C(S)\,N(H)$, $(H)\,NC(S)$, $S(O)_2N(H)$, $N(H)\,S(O)_3$, $S(O)_2N(H)\,C(O)$, and $C(O)\,N(H)\,S(O)_3$;

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 Y° is phenyl or a heteroaryl of 5 or 6 ring members, wherein one carbon of said phenyl or said heteroaryl is substituted by Q° , a carbon two or three contiguous atoms from the point of attachment of Q° to said phenyl or said heteroaryl 1s substituted by Q° , a carbon adjacent to the point of attachment of Q° is optionally substituted by $R^{1\circ}$, another carbon adjacent to the point of attachment of Q° is optionally substituted by $R^{1\circ}$, a carbon adjacent to Q° is optionally substituted by $R^{1\circ}$, and another carbon adjacent to Q° is optionally substituted by $R^{1\circ}$, and another carbon adjacent to Q° is optionally substituted by $R^{1\circ}$,

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Ris, Rir, Ris, and Ris are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, nitro, alkoxyamino, alkylamino, alkylthio, alkylsulfinyl, alkanoyl, haloalkanoyl, alkyl, alkenyl, halo, haloalkoxyalkyl, aminoalkyl, haloalkoxy, nydroxyalkyl, aminoalkyl, haloalkoxy, and cyano;

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R¹⁶ or R¹⁹ is optionally selected from the group consisting of NR²⁰R²¹, N(R²⁶)C(NR²⁵)N(R²¹) (R²⁴), and C(NR²⁵)NR²³R²⁴, with the proviso that R¹⁶, R¹⁹, and Q⁵ are not simultaneously hydrido;

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 Q^{2} is selected from the group consisting of $NR^{2}R^{21}$, aminoalkyl, hydrido, $N(R^{26})C(NR^{25})N(R^{23})$ (R^{24}), and $C(NR^{25})NR^{25}R^{24}$, with the proviso that no more than one of R^{20}

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and R^{21} is selected from the group consisting of hydroxy, amino, alkylamino, and dialkylamino at the same time, with the further proviso that no more than one of R^{21} and R^{24} is selected from the group consisting of hydroxy, amino, alkylamino, and dialkylamino at the same time;

R¹⁰, R¹¹, R¹³, R¹⁵, R¹⁵, and R¹⁶ are independently selected from the group consisting of hydrido, alkyl, hydroxy, aminoalkyl, amino, dialkylamino, alkylamino, and hydroxyalkyl;

 $(CR^3)^R^{11})_b$ wherein b is an integer selected from 1 through 4, and $(CH(R^{14}))_c - W^2 - (CH(R^{15}))_d$ wherein c and d are integers independently selected from 1 through 3 and W^1 is selected from 1 through 3 and W^1 is selected from 1 through 3 and W^1 is selected from 0 through 3 and W^1 is selected from other than halo when directly bonded to N, and with the additional proviso that $(CR^{3})^R^{3}$, and $(CH(R^{14}))_c$ are bonded to E^c ;

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 Y^o is optionally Q^b-Q^{aa} wherein Q^{aa} is $(CH(R^{14}))_b^{aa}-W^{aa}$ $(CH(R^{15}))_b$, wherein a and b are independently 1 or 2 and W^a is $CR^{aa}=CR^{aa}$, with the proviso that $(CH(R^{14}))_b^a$ is bonded to E^o .

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In a more preferred embodiment of a compound of Formula I, said compound is the Formula:

or a pharmaceutically acceptable salt thereof, wherein; M is N or $N\!\!\to\!\!0;$

Wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to A is optionally substituted by R¹³, the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R³⁴, a carbon adjacent to R³⁴ and two atoms from the carbon at the point of attachment is optionally substituted by R³⁴, a carbon adjacent to R³⁴ and two atoms from the carbon at the point of attachment is optionally substituted by R³⁴, a carbon adjacent to R³⁴ and two atoms from the carbon at the point of attachment is optionally substituted by R³⁴, and any carbon adjacent to both R³⁴ and R³⁵ is optionally substituted by R³⁴;

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R²³, R²⁴, R²⁴, and R²⁴ are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkylenedioxy, haloalkylthio, alkanoyloxy, alkoxy, hydroxy, amino, arkoxyamino, haloalkanoyl, nitro, alkylamino, alkylthio, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, alkylsulfonamido, amidosulfonyl, alkyl, alkenyl, haloa, haloalkyl, haloalkenyl, haloalkoxy, carboxy, carboxamido, cyano, and Q^b;

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B is optionally selected from the group consisting of hydrido, trialkylsilyl, C2-C8 alkyl, C3-C8 alkylenyl, C3-C8 alkenyl, C3-C8 alkynyl, and C2-C8 haloalkyl, wherein each member of group B is optionally substituted at any carbon up to and including 6 atoms from the point of attachment of B to A with one or more of the group consisting of R¹², R¹³, R¹⁴, R¹⁵, and R¹⁵;

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B is optionally a C3-C12 cycloalkyl or a C4-C9 saturated heterocyclyl, wherein each ring carbon is optionally substituted with \mathbb{R}^{13} , a ring carbon other than the ring carbon at the point of attachment of B to A is optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same

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time, ring carbons and a nitrogen adjacent to the carbon atom at the point of attachment are optionally substituted with R° or R¹¹, a ring carbon or nitrogen atom adjacent to the R° position and two atoms from the point of attachment is optionally substituted with R¹¹, a ring carbon or nitrogen atom adjacent to the R¹¹ position and two atoms from the point of attachment is optionally substituted with R¹², a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R¹¹ position is optionally substituted with R¹¹, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R¹¹ position is optionally substituted with R³¹, and a ring carbon or nitrogen atom four atoms from the point of attachment and adjacent to the R¹¹ and R³¹ positions is optionally substituted with R³¹,

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R, R10, R11, R12, and R11 are independently selected from the group consisting of hydrido, acetamido, haloacetamido, alkoxyamino, alkanoyl, haloalkanoyl, amidino, guanidino, alkylenedioxy, haloalkylthio, alkoxy, cycloalkoxy, aralkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, heterocyclyloxy, heterocyclylakoxy, hydroxy, amino, alkylamino, N-alkylovarylamino, arylamino, aralkylamino, heteroaralkylamino, heteroarylyamino, heteroaralkylamino,

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heterocyclylalkylamino, alkylthio, alkylsulfinyl, arylsulfinyl, arylsulfinyl, aralkylsulfinyl, cycloalkylsulfinyl, heteroarylsulfinyl, alkylsulfonyl, arylsulfonyl, cycloalkylsulfonyl, heteroarylsulfonyl, amidosulfonyl, alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, halo, haloshkyl, maloalkyl, hydroxyalkyl, hydroxyalkyl, carboxyalkyl, carboxyalkyl, carboxyalkyl, carboxyalkyl, and cyano;

30

A is a bond or $(CH(R^{15}))_{pa}-(W^7)_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W' is selected from the group consisting of 0, S, C(0),

 $(R^7)NC(O)$, $(R^7)NC(S)$, and $N(R^7)$, with the proviso that W^7 is bonded to the N(H) on the pyridine ring; R' is selected from the group consisting of hydrido, hydroxy and alkyl;

R15 is selected from the group consisting of hydrido, hydroxy, halo, alkyl, and haloalkyl;

S

Ja is N or C-X';

Jb is N or C-R1;

hydroxy, hydroxyamino, alkoxy, hydroxyalkyl, alkoxyamino, R^1 and X^0 are independently selected from the group consisting of hydrido, alkyl, cyano, halo, haloalkyl, haloalkoxy, amino, aminoalkyl, alkylamino, amidino, thiol, and alkylthio;

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wherein -W=X-Y=Z- forms an aryl or heteroaryl of 5 or X° and R¹ or R¹ and R² is optionally -W=X-Y=Zring-members;

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group consisting of C(R*), C(R10), C(R11), C(R12), N, N(R10), O, S and a bond with the proviso that one of W, X, Y, and X, Y, and Z is O or S, with the further proviso that no W, X, Y, and Z are independently selected from the Z is independently selected to be a bond when one of W, more than one of W, X, Y, and Z is optionally selected additional proviso that no more than three of W, X, Y, from the group consisting of O and S, and with the and Z are optionally N or N(R10);

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to form C5-C8 cycloalkenyl ring or a partially saturated X° and R¹ or R¹ and R² is optionally bonded together C5-C8 heterocyclyl ring, wherein said cycloalkenyl ring or heterocyclyl ring is optionally substituted with one or more of the group consisting of R3, R10, R11, R12, and

R2 is Z0-Q;

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wherein g and p are integers independently selected from Z° is selected from the group consisting of a bond, $\left(CR^{41}R^{42}\right)_q$ wherein q is 1 or 2, and $\left(CH\left(R^{41}\right)\right)_g-W^0-\left(CH\left(R^{42}\right)\right)_p$

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0 through 3 and W° is selected from the group consisting

 Z^{0} is optionally (CH(R⁴¹)),-W²²-(CH(R⁴²)), wherein e and of O, S, C(O), S(O), N(R41), and ON(R41);

h are independently 0 or 1 and W^{23} is selected from the pyrrolidinyl, 2,3-pyrrolidinyl, 2,4-pyrrolidinyl, 2,5-2,4-tetrahydrofuranyl, 2,5-tetrahydrofuranyl, and 3,4pyrrolidinyl, 3,4-pyrrolidinyl, 2,3-tetrahydrofuranyl, piperazinyl, 2,6-piperazinyl, 1,2-piperidinyl, 1,3cyclopentyl, 1,3-cyclopentyl, 2,3-morpholinyl, 2,4piperidinyl, 2,3-piperidinyl, 2,4-piperidinyl, 2,6piperidinyl, 3,4-piperidinyl, 1,2-pyrrolidinyl,1,3morpholinyl, 2,6-morpholinyl, 3,4-morpholinyl, 3,5morpholinyl, 1,2-piperazinyl, 1,3-piperazinyl, 2,3group consisting of CR"=CR", 1,2-cyclopropyl, 1,2cyclobutyl, 1,2-cyclohexyl, 1,3-cyclohexyl, 1,2-

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pyridine ring and W²² is optionally substituted with one or tetrahydrofuranyl, wherein 2° is directly bonded to the more substituents selected from the group consisting of R, R10, R11, R12, and R13;

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R'1 and R'2 are independently selected from the group

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optionally substituted by R³, the other carbon adjacent to substituted by \mathbb{R}^{12} , and any carbon adjacent to both \mathbb{R}^{10} and substituted by R10, a carbon adjacent to R13 and two atoms from the carbon at the point of attachment is optionally from the carbon at the point of attachment is optionally Q is phenyl or a heteroaryl of 5 or 6 ring members, substituted by R11, a carbon adjacent to R9 and two atoms wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to 2° is the carbon at the point of attachment is optionally consisting of hydrido, hydroxy, alkyl, and amino; R¹² is optionally substituted by R¹¹;

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Q is optionally hydrido with the proviso that Z° is other than a bond;

R** and R** are independently selected from the group consisting of hydrido, hydroxyalkyl, alkyl, alkoxyalkyl, alkylthioalkyl, and haloalkyl;

 E^0 , with the proviso that K is CR^4R^4b , is E^1 wherein E^1 is selected from the group consisting of a covalent single bond, C(0)N(H), (H)NC(0), $S(0)_2N(H)$, and $N(H)S(0)_2$,

K is optionally $(CH(R^{14}))_j$ -T wherein j is 0 or 1 and T is a bond or $N(R^7)$ with the proviso that $(CH(R^{14}))_j$ is bonded to the phenyl ring;

bonded to the phenyl ring; R14 is hydrido or halo;

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 $E^{o},$ with the proviso that K is $(CH(R^{14}))_{3}-T,$ is E^{2} wherein E^{2} is selected from the group consisting of $C(O)\,N(H)$, $(H)\,NC(O)$, $C(S)\,N(H)$, $(H)\,NC(S)$, $S(O)_{2}N(H)$, $N(H)\,S(O)_{2},$ $S(O)_{2}N(H)\,C(O)$, and $C(O)\,N(H)\,S(O)_{2};$

y° is phenyl or a heteroaryl of 5 or 6 ring members, wherein one carbon of said phenyl or said heteroaryl is substituted by Q°, a carbon two or three atoms from the point of attachment of Q° to said phenyl or said heteroaryl is substituted by Q°, a carbon adjacent to the point of attachment of Q° is optionally substituted by R¹¹, another carbon adjacent to the point of attachment of Q° is optionally substituted by R¹³, a carbon adjacent to Q° is optionally substituted by R¹³, and another carbon adjacent to Q° is optionally substituted by R¹³,

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Ris, Ri', Ris, and Ris are independently selected from the group consisting of hydrido, amidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and

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R¹⁶ or R¹⁹ is optionally selected from the group consisting of NR²⁰R²¹, N(R26)C(NR25)N(R23)(R²⁴), and C(NR²⁵)NR²¹R²¹, with the proviso that R¹⁶, R¹⁹, and Q^b are not simultaneously hydrido;

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 Q^b is selected from the group consisting of $NR^{2n}R^{2n}$, hydrido, $N(R^{2n})C(NR^{2n})N(R^{2n})$, (R^{2n}) , and $C(NR^{2n})NR^{2n}R^{2n}$, with the proviso that no more than one of R^{2n} and R^{2n} is selected from the group consisting of hydroxy, amino, alkylamino, and dialkylamino at the same time, with the further proviso that no more than one of R^{2n} and R^{2n} is selected from the group consisting of hydroxy, amino, alkylamino, and dialkylamino at the same time;

R²⁰, R²¹, R²⁴, R²⁴, R²⁵, and R²⁶ are independently selected from the group consisting of hydrido, alkyl, hydroxy, amino, alkylamino and dialkylamino;

10

Q* is selected from the group consisting of a bond, (CR,³/₈), wherein b is an integer selected from 1 through 4, and (CH(R¹⁴))_c-W¹⁻(CH(R¹⁵))_d wherein c and d are integers independently selected from 1 through 3 and W¹ is selected from the group consisting of C(O)N(R¹⁴), (R¹⁴)NC(O), S(O), S(O)₂, S(O)2N(R¹⁴), N(R¹⁴)S(O)₂, and N(R¹⁴), with the proviso that R¹⁴ is selected from other than halo when directly bonded to N, and with the additional proviso that (CR³/₁₈)_b and (CR³/₁₈)_b, and (CH(R¹⁴))_c are bonded to B⁰;

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Consisting of hydrido, alkyl, and haloalkyl;

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R¹⁸ is optionally aroyl or heteroaroyl, wherein R¹⁸ is optionally substituted with one or more substituents selected from the group consisting of R¹⁶, R¹⁷, R¹⁸, and

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 Y^0 is optionally Y^{AT} wherein Y^{AT} is $Q^b - Q^a$; Y^0 is optionally $Q^b - Q^{aa}$ wherein Q^{aa} is $(CH(R^{15}))_h$, wherein a and b are independently 1 or 2 and b^a is $CR^{4a} - CR^{4b}$ with the proviso that $(CH(R^{14}))_{\bullet}$ is bonded to E^0 .

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In an even more preferred embodiment of a compound of Formula I, said compound is the Formula:

or a pharmaceutically acceptable salt thereof, wherein, M is N or N>O;

B is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to A is optionally substituted by R¹³, the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R¹⁶, a carbon adjacent to R¹² and two atoms from the carbon at the point of attachment is optionally substituted by R¹³, a carbon adjacent to R¹⁶ and two atoms from the carbon at the point of attachment is optionally substituted by R¹⁵, and any carbon adjacent to both R¹³ and R¹⁵ is optionally substituted by R¹⁵,

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R¹², R¹³, R¹³, and R¹⁶ are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkoxy, hydroxy, amino, alkoxyamino, alkylamino, alkylthio, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, hydroxyhaloalkyl, carboalkoxy, carboxy, carboxamido, cyano, and Q^b;

15

A is a bond or $(CH(R^{15}))_{pa}$ - $(W^2)_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W² is $(R^2)NC(0)$ or $N(R^2)$;

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R) is selected from the group consisting of hydrido, hydroxy and alkyl; R¹⁵ is selected from the group consisting of hydrido, halo, alkyl, and haloalkyl;

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Ja is N or C-X°; Jb is N or C-R¹;

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R¹ and X° are independently selected from the group consisting of hydrido, hydroxy, hydroxyamino, amidino, amino, cyano, hydroxyalkyl, alkoxy, alkyl, alkylamino, aminoalkyl, alkylthio, alkoxyamino, haloalkyl,

haloalkoxy, and halo;

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R2 is Z0-Q;

 Z^o is selected from the group consisting of a bond, $CH_2, CH_2CH_2, \ W^o-(CH(R^{12}))_{\mathfrak{p}}$ wherein p is 0 or 1 and W^o is

selected from the group consisting of O, S, and N(R'1); R'1 and R'2 are independently hydrido or alkyl;

2

Q is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to 2° is optionally substituted by R, the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R¹³, a carbon adjacent to R, and two atoms from the carbon at the point of attachment is optionally substituted by R¹³, a carbon adjacent to R¹³ and two atoms from the carbon at the point of attachment is optionally substituted by R¹³, and any carbon adjacent to both R¹⁰ and R¹³ is optionally substituted by R¹³;

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R, R11, and R13 are independently selected from the group consisting of hydrido, hydroxy, amino, amidino, guanidino, alkylamino, alkylthio, alkylsulfonamido, alkylsulfinyl, alkylsulfonyl, amidosulfonyl, alkyl, alkoxy, halo, haloalkyl, haloalkoxy, hydroxyalkyl, hydroxyhaloalkyl, carboxy, carboxamido, and cyano;

25

R¹⁰ and R¹³ are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkyl, aryl, aralkyl, cycloalkyl, cycloalkyl, heteroaryl, heterocyclyl, alkoxy, cycloalkoxy, cycloalkoxy, aralkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclylalxoxy, heterocyclylalkoxy, hydroxy, amino, alkoxyamino, alkylamino, arylamino, aralkylamino, heteroaralkylamino, heterocyclylamino,

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wherein one carbon of said phenyl or said heteroaryl is substituted by Q^* , a carbon two or three atoms from the point of attachment of Q^* to said phenyl or said heteroaryl is substituted by Q^b , a carbon adjacent to the point of attachment of Q^* is optionally substituted by R^{17} , another carbon adjacent to the point of attachment of Q^* is optionally substituted by R^{18} , a carbon adjacent to Q^* is optionally substituted by R^{18} , and another carbon adjacent to Q^b is optionally substituted by R^{18} , and another carbon adjacent to Q^b is optionally substituted by R^{18} , and another carbon adjacent to Q^b is optionally substituted by R^{18} ,

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the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, alkylthio, alkylsulfinyl, alkylsulfinyl, alkanoyl, haloalkanoyl, alkylsulfinyl, haloalky, hydroxyalkyl, aminoalkyl, and cyano, haloalky, hydroxyalkyl, aminoalkyl, and cyano;

20

 R^{16} or R^{19} is optionally $NR^{20}R^{21}$ or $C(NR^{25})\,NR^{29}R^{24}$, with the proviso that $R^{16},\ R^{19},\$ and Qb are not simultaneously hydrido;

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 Q^b is selected from the group consisting of NR²⁰R²¹, hydrido, and C(NR²⁵)NR²¹R²⁴, with the proviso that no more than one of R²⁰ and R²¹ is hydroxy at the same time and with the further proviso that no more than one of R²¹ and R²⁴ is hydroxy at the same time;

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R²⁰, R²¹, R²¹, R²⁴, and R²⁵ are independently selected from the group consisting of hydrido, alkyl, and hydroxy; Q^e is selected from the group consisting of a bond,

In another even more preferred embodiment of a compound of Formula I, said compound is the Formula:

CH2, and CH2CH1.

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or a pharmaceutically acceptable salt thereof, wherein;

M is N or N→O;

B is selected from the group consisting of hydrido, C2-C8 alkyl, C3-C8 alkynyl, and C2-C8 haloalkyl, wherein each member of group B is optionally substituted at any carbon up to and including 6 atoms from the point of attachment of B to A with one or more of the group consisting of R²³, R²⁴, R²⁴, R³⁵, and R³⁶,

R¹³, R¹³, R¹³, and R¹⁶ are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkoxy, hydroxy, amino, alkoxyamino, alkylamino, alkylthio, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, hydroxyhaloalkyl, carboalkoxy, carboxy, carboxamido, cyano, and Q⁵;

10

A is a bond or $(CH(R^{15}))_{pa}-(W^7)_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W is $(R^7)NC(0)$ or $N(R^7)$;

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 $\ensuremath{R^{7}}$ is selected from the group consisting of hydrido, hydroxy and alkyl;

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 \mathbb{R}^{15} is selected from the group consisting of hydrido, halo, alkyl, and haloalkyl;

Ja is Nor C-X';

Jb is N or C-R1;

25

R¹ and X° are independently selected from the group consisting of hydrido, hydroxy, hydroxyamino, amidino, amino, cyano, hydroxyalkyl, alkoxy, alkyl, alkylamino, aminoalkyl, alkylthio, alkoxyamino, haloalkyl, and halo;

R2 is Z0-Q;

 Z^o is selected from the group consisting of a bond, $CH_2, CH_2CH_2, \ W^o-(CH(R^{42}))_p$ wherein p is 0 or 1 and W^o is selected from the group consisting of 0, S, and $N(R^{41})_r$

R*1 and R*2 are independently hydrido or alkyl;

Q is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to Z^{0} is optionally substituted by R^{3} , the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R^{13} , a carbon adjacent to R^{0} and two atoms from the carbon at the point of attachment is optionally substituted by R^{10} , a carbon adjacent to R^{13} and two atoms from the carbon at the point of attachment is optionally substituted by R^{13} , and any carbon adjacent to both R^{10} and R^{12} is optionally substituted by R^{11} ;

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R³, R¹¹, and R¹³ are independently selected from the group consisting of hydrido, hydroxy, amino, amidino, guanidino, alkylamino, alkylthio, alkylsulfonamido, alkylsulfinyl, alkylsulfonyl, amidosulfonyl, alkyl, alkoxy, halo, haloalkyl, haloalkoxy, hydroxyalkyl, hydroxyhaloalkyl, carboxy, carboxamido, and cyano;

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R¹⁰ and R¹² are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkyl, aryl, aralkyl, cycloalkyl cycloalkyl, heterocyclyl, alkoxy, cycloalkylalkoxy, aralkoxy, aryloxy, heteroaryloxy, heterocyclyloxy, heterocyclyloxy, heterocyclylakoxy, hydroxy, amino, alkoxyamino, alkylamino, arylamino, aralkylamino, heterocyclylamino, heterocyclylamino, heterocyclylamino, heterocyclylamino, heterocyclylamino, heterocyclylamino, arylsulfinyl, aralkylsulfinyl, cycloalkylsulfinyl, arylsulfinyl, aralkylsulfinyl, aralkylsulfonyl, aralkylsulfinyl, aralkylsulfonyl, aralkylsulfonyl, aralkylsulfonyl, aralkylsulfonyl, aralkylsulfonyl, aralkylsulfonyl, aralkylsulfonyl, aralkylsulfonyl,

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sycloalkylsulfonyl, heteroarylsulfonyl, hydroxyalkyl,

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hydroxyhaloalkyl, aminoalkyl, carboalkoxy, carboxy, carboxyalkyl, carboxamido, halo, haloalkyl, and cyano;

v° is phenyl or a heteroaryl of 5 or 6 ring members, wherein one carbon of said phenyl or said heteroaryl is substituted by 0°, a carbon two or three atoms from the point of attachment of 0° to said phenyl or said heteroaryl is substituted by 0°, a carbon adjacent to the point of attachment of 0° is optionally substituted by R'', another carbon adjacent to the point of attachment of 0° is optionally substituted by R''s, a carbon adjacent to 0° is optionally substituted by R''s, and another carbon adjacent to 0° is optionally substituted by R''s,

10

Ri⁶, Ri⁷, Ri⁸, and Ri⁸ are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano;

12

R¹⁶ or R¹⁹ is optionally selected from the group consisting of NR²⁹, N(R²⁶)C(NR²⁵)N(R²³) (R²⁴), and C(NR²⁵)NR²³R²⁴, with the proviso that R¹⁶, R¹⁹, and Q^b are not simultaneously hydrido;

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 Q^b is selected from the group consisting of $NR^{20}R^{21}$, hydrido, $C(NR^{25})NR^{21}R^{21}$, and $N(R^{26})C(NR^{25})N(R^{21})$ (R^{24}), with the proviso that no more than one of R^{20} and R^{21} is hydroxy at the same time and with the further proviso that no more than one of R^{23} and R^{24} is hydroxy at the same time;

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R²⁰, R²¹, R²³, R²⁴, R²⁵, and R²⁶ are independently selected from the group consisting of hydrido, alkyl, and hydroxy;

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O' is selected from the group consisting of a bond, CH2, and CH2CH3.

In still another even more preferred embodiment of a compound of Formula I, said compound is the Formula:

or a pharmaceutically acceptable salt thereof, wherein, M is N or $N\!\to\! O;$

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atoms from the point of attachment and adjacent to the \mathtt{R}^{12} carbons and a nitrogen adjacent to the carbon atom at the carbon at the point of attachment of B to A is optionally point of attachment are optionally substituted with R9 or R13, a ring carbon or nitrogen adjacent to the R9 position attachment and adjacent to the R10 position is optionally substituted with oxo provided that no more than one ring and two atoms from the point of attachment is optionally substituted with R10, a ring carbon or nitrogen adjacent position is optionally substituted with R11, and a ring substituted with R13, a ring carbon other than the ring attachment is optionally substituted with R12, a ring substituted with R11, a ring carbon or nitrogen three attachment and adjacent to the R11 and R33 positions is heterocyclyl, wherein each ring carbon is optionally carbon is substituted by oxo at the same time, ring to the R13 position and two atoms from the point of B is a C3-C7 cycloalkyl or a C4-C6 saturated carbon or nitrogen three atoms from the point of carbon or nitrogen four atoms from the point of optionally substituted with R34;

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R, R11, and R11 are independently selected from the group consisting of hydrido, hydroxy, amino, amidino, guanidino, alkylamino, alkylthio, alkylsulfonamido, alkylsulfinyl, alkylsulfonyl, amidosulfonyl, alkyl, alkoxy, halo, haloalkyl, haloalkoxy, hydroxyalkyl, hydroxyhaloalkyl, carboxy, carboxamido, and cyano;

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R10 and R12 are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkyl, aryl, aralkyl, cycloalkyl, cycloalkyl, heteroaryl, heterocyclyl, alkoxy, cycloalkylalkoxy, aralkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, aralkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, amino, alkoxyamino, alkylamino, arylamino, aralkylamino, aralkylamino, heteroarylamino,

heteroaralkylamino, heterocyclylamino, heterocyclylalkylamino, alkylsulfonamido, amidosulfonyl, arylsulfinyl, aralkylsulfinyl, cycloalkylsulfinyl, heteroarylsulfinyl, arylsulfonyl, aralkylsulfonyl, cycloalkylsulfonyl, heteroarylsulfonyl, hydroxyalkyl, hydroxyhaloalkyl, aminoalkyl, carboalkoxy, carboxy, carboxyalkyl, carboxamido, halo, haloalkyl, and cyano;

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R³³ and R³⁴ are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkoxy, hydroxy, amino, alkoxyamino, alkylthio, amidosulfonyl, alkyl, halo, haloalkoxy, hydroxyalkyl, hydroxyhaloalkyl, carboxy, carboxamido, and cyano;

R33 is optionally Qb;

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A is a bond or $(CH(R^{15}))_{pa}-(W^7)_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W⁷ is $(R^7)NC(0)$ or $N(R^7)$;

25

 $\ensuremath{\mathrm{R}}^{\gamma}$ is selected from the group consisting of hydrido, hydroxy and alkyl;

R¹⁵ is selected from the group consisting of hydrido, halo, alkyl, and haloalkyl;

Ja is Nor C-X°;

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Jb is N or C-R1;

R¹ and X° are independently selected from the group consisting of hydrido, hydroxy, hydroxyamino, amidino, amino, cyano, hydroxyalkyl, alkoxy, alkyl, alkylamino, aminoalkyl, alkylthio, alkoxyamino, haloalkyl,

haloalkoxy, and halo;

R is Z0-0;

 Z^o is selected from the group consisting of a bond, CH_2 , CH_2CH_2 , W^- ($CH(R^{43})$), wherein p is 0 or 1 and W^o is selected from the group consisting of 0, S, and $N(R^{41})$; R^{41} and R^{42} are independently hydrido or alkyl;

Q is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to \mathbf{Z}^0 is optionally substituted by R^1 , the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R^{13} , a carbon adjacent to R^2 and two atoms from the carbon at the point of attachment is optionally substituted by R^{19} , a carbon adjacent to R^{13} and two atoms from the carbon at the point of attachment is optionally substituted by R^{12} , and any carbon adjacent to both R^{19} and R^{12} is optionally substituted by R^{11} ;

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y° is phenyl or a heteroaryl of 5 or 6 ring members, wherein one carbon of said phenyl or said heteroaryl is substituted by Q°, a carbon two or three atoms from the point of attachment of Q° to said phenyl or said heteroaryl is substituted by Q°, a carbon adjacent to the point of attachment of Q° is optionally substituted by R¹¹, another carbon adjacent to the point of attachment of Q° is optionally substituted by R¹¹, a carbon adjacent to Q° is optionally substituted by R¹¹, and another carbon adjacent to Q° is optionally substituted by R¹¹,

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Rif, Ri', Rig, and Rig are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano;

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 R^{16} or R^{19} is optionally $NR^{20}R^{21}$ or and $C(NR^{25})NR^{23}R^{24}$, with the proviso that R^{16} , R^{19} , and Q^b are not simultaneously hydrido;

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 Q^b is selected from the group consisting of $NR^{20}R^{21}$, hydrido, and $C(NR^{25})NR^{23}R^{24}$, with the proviso that no more than one of R^{20} and R^{21} is hydroxy at the same time and with the further proviso that no more than one of R^{23} and R^{24} is hydroxy at the same time;

R", R", R", R", and R" are independently selected from the group consisting of hydrido, alkyl, and hydroxy; Q" is selected from the group consisting of a bond, CH, and CH,CH,.

In an additional even more preferred embodiment of compound of Formula I, said compound is the Formula:

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or a pharmaceutically acceptable salt thereof, wherein; M is N or N $\rightarrow 0$;

B is selected from the group consisting of hydrido, trialkylsilyl, C2-C4 alkyl, C3-C5 alkylenyl, C3-C4 alkenyl, C3-C4 alkynyl, and C2-C4 haloalkyl, wherein each member of group B is optionally substituted at any carbon up to and including 3 atoms from the point of attachment of B to A with one or more of the group consisting of \mathbb{R}^{13} , and \mathbb{R}^{14} ;

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R¹³, R¹³, and R¹⁴ are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkoxy, hydroxy, amino, alkoxyamino, alkylamino, alkylthio, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, hydroxyhaloalkyl, carboxy, carboxy, carboxamido, and cyano;

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A is (CH(R¹⁵))_{ps}-N(R⁷) wherein pa is an integer selected from 0 through 2 and R⁷ is hydrido or alkyl;
R¹⁵ is selected from the group consisting of hydrido, halo, alkyl, and haloalkyl;

Ja is Nor C-Xº;

Jb is N or C-R1;

R¹ and X° are independently selected from the group consisting of hydrido, alkyl, cyano, halo, haloalkyl, haloalkoxy, amino, aminoalkyl, alkylamino, amidino, hydroxy, hydroxyamino, alkoxy, hydroxyalkyl, alkoxyamino, thiol, and alkylthio;

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R2 is Z0-Q;

Z° is a bond or CH2;

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Q is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to \mathbf{Z}^0 is optionally substituted by \mathbf{R}^3 , the other carbon adjacent to the carbon at the point of attachment is optionally substituted by \mathbf{R}^{13} , a carbon adjacent to \mathbf{R}^9 and two atoms from the carbon at the point of attachment is optionally substituted by \mathbf{R}^{19} , a carbon adjacent to $\mathbf{R}13$ and two atoms from the carbon at the point of attachment is optionally substituted by \mathbf{R}^{19} , and any carbon adjacent to both \mathbf{R}^{19} and \mathbf{R}^{19} is optionally substituted by \mathbf{R}^{11} ;

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R, R11, and R13 are independently selected from the group consisting of hydrido, hydroxy, amino, amidino, guanidino, alkylamino, alkylthio, alkylsulfonmamido, alkylsulfinyl, alkylsulfonyl, amidosulfonyl, alkyl, alkxy, halo, haloalkyl, haloalkoxy, hydroxyalkyl, hydroxyhaloalkyl, carboxy, carboxamido, and cyano;

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R¹⁰ and R¹² are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkyl, aryl, aralkyl, cycloalkylalkyl, cycloalkylalkyl, heterocyclyl, alkoxy, cycloalkoxy, cycloalkoxy, aralkoxy, aryloxy, heteroaryloxy, heterocyclyloxy, heterocyclylalkoxy, hydroxy, amino, alkoxyamino, alkylamino, arylamino, aralkylamino, heteroaralkylamino, heterocyclylamino, heterocyclylamino, heterocyclylamino, heterocyclylamino, alkylsulfonamido, amidosulfonyl, heterocyclylalkylamino, alkylsulfonamido, amidosulfonyl,

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arylsulfinyl, aralkylsulfinyl, cycloalkylsulfinyl, heteroarylsulfinyl, arylsulfonyl, aralkylsulfonyl, cycloalkylsulfonyl, heteroarylsulfonyl, hydroxyalkyl, hydroxyhaloalkyl, aminoalkyl, carboxlkoxy, carboxy, carboxyalkyl, carboxyalkyl, and cyano;

 Y^0 is phenyl or a heteroaryl of 5 or 6 ring members, wherein one carbon of said phenyl or said heteroaryl is substituted by Q^* , a carbon two or three atoms from the point of attachment of Q^* to said phenyl or said heteroaryl is substituted by Q^* , a carbon adjacent to the point of attachment of Q^* is optionally substituted by R^{17} , another carbon adjacent to the point of attachment of Q^* is optionally substituted by R^{19} , a carbon adjacent to Q^* is optionally substituted by R^{19} , and another carbon adjacent to Q^* is optionally substituted by R^{19} , and another carbon adjacent to Q^* is optionally substituted by R^{19} ,

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Rif, Ri¹, and Ri⁹ are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, alkylaulfinyl, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano;

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R¹⁶ or R¹⁹ is optionally selected from the group consisting of NR²⁰R²¹, N(R²⁶)C(NR²⁵)N(R²³) (R²⁴), and C(NR²⁵)NR²³R²³, with the proviso that R¹⁶, R¹⁹, and Q⁹ are not simultaneously hydrido;

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Q⁵ is selected from the group consisting of NR²⁰R²¹, hydrido, C(NR²³)NR²¹R²⁴, and N(R²⁴)C(NR²³)N(R²³) (R²⁴), with the proviso that no more than one of R²⁰ and R²¹ is hydroxy at the same time and with the further proviso that no more than one of R²³ and R²⁴ is hydroxy at the same time;

R²⁰, R²¹, R²³, R²⁴, R²⁴, and R²⁴ are independently selected from the group consisting of hydrido, alkyl, and

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hydroxy;

Q* is selected from the group consisting of a bond,
CH,, and CH,CH,.

In a fifth even more preferred embodiment of a compound of Formula I, said compound is the Formula:

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or a pharmaceutically acceptable salt thereof, wherein, M is N or $N\!\!\to\!\!O,$

B is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to A is optionally substituted by R¹³, the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R¹⁶, a carbon adjacent to R¹³ and two atoms from the carbon at the point of attachment is optionally substituted by R¹³, a carbon adjacent to R¹⁶ and two atoms from the carbon at the point of attachment is optionally substituted by R¹⁵, and any carbon adjacent to both R¹³ and R¹⁵ is optionally substituted by R¹⁵;

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R²³, R²¹, R²¹, and R²⁴ are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkylenedioxy, haloalkylthio, alkanoyloxy, alkoxy, hydroxy, amino, alkoxyamino, haloalkanoyl, nitro, alkylamino, alkylthio, aryl, aralkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, alkylsulfonamido, amidosulfonyl, alkyl, alkenyl, haloalkenyl, haloalkoxy, hydroxyalkyl, alkylamino, carboalkoxy, carboxy, carboxy, and Q⁵;

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B is optionally selected from the group consisting of hydrido, trialkylsilyl, C2-C8 alkyl, C3-C8 alkylenyl, C3-C8 alkenyl, C3-C8 alkenyl, and C2-C8 haloalkyl, wherein each member of group B is optionally substituted at any carbon up to and including 6 atoms from the point

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of attachment of B to A with one or more of the group consisting of R^{12} , R^{13} , R^{15} , and R^{16} ;

adjacent to the R12 position is optionally substituted with position is optionally substituted with R11, a ring carbon atoms from the point of attachment and adjacent to the \mathtt{R}^{10} optionally substituted with R33, a ring carbon other than or nitrogen three atoms from the point of attachment and time, ring carbons and a nitrogen adjacent to the carbon adjacent to the R' position and two atoms from the point of attachment is optionally substituted with R10, a ring the ring carbon at the point of attachment of B to A is carbon or nitrogen adjacent to the R13 position and two than one ring carbon is substituted by oxo at the same R13, and a ring carbon or nitrogen four atoms from the substituted with R12, a ring carbon or nitrogen three optionally substituted with oxo provided that no more substituted with R° or R13, a ring carbon or nitrogen B is optionally a C3-C12 cycloalkyl or a C4-C9 saturated heterocyclyl, wherein each ring carbon is point of attachment and adjacent to the R^{11} and R^{33} atoms from the point of attachment is optionally atom at the point of attachment are optionally positions is optionally substituted with R¹⁴;

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R, R, R, RH, and R, are independently selected from the group consisting of hydrido, acetamido, haloacetamido, alkoxyamino, alkanoyl, haloalkanoyl, amidino, guanidino, alkylenedioxy, haloalkylthio, alkoxy, cycloalkoxy, cycloalkoxy, aralkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, amino, alkylamino, N-alkyl-N-arylamino, arylamino, aralkylamino, heteroarylamino, heterocyclylamino, heterocyclylamino, heterocyclylamino, alkylthio, alkylsulfinyl, arylsulfinyl, aralkylsulfinyl, cycloalkylsulfinyl, heteroarylsulfinyl, aralkylsulfinyl, cycloalkylsulfinyl, arylsulfonyl, aralkylsulfonyl, cycloalkylsulfonyl, arylsulfonyl, aralkylsulfonyl, cycloalkylsulfonyl,

heteroarylsulfonyl, amidosulfonyl, alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, hydroxyhaloalkyl, aminoalkyl, carboalkoxy, carboxy, halo, haloalkyl, haloalkoxy, hydroxyalkyl, carboxyalkyl, carboxamido, and cyano;

A is a bond or $(CH(\mathbb{R}^{19}))_{pa}$ - $(W^7)_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W' is selected from the group consisting of 0, S, C(0), $(R^7)NC(O)$, $(R^7)NC(S)$, and $N(R^7)$;

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R15 is selected from the group consisting of hydrido, R' is selected from the group consisting of hydrido, hydroxy and alkyl;

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hydroxy, halo, alkyl, and haloalkyl;

Ja is N or C-X';

Jb is N or C-R1;

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hydroxy, hydroxyamino, alkoxy, hydroxyalkyl, alkoxyamino, R^1 and X° are independently selected from the group consisting of hydrido, alkyl, cyano, halo, haloalkyl, haloalkoxy, amino, aminoalkyl, alkylamino, amidino, thiol, and alkylthio;

wherein g and p are integers independently selected from $(CR^{41}R^{42})_q$ wherein q is 1 or 2, and $(CH\left(R^{41}\right))g-W^0-\left(CH\left(R^{42}\right)\right)_p$ 0 through 3 and W° is selected from the group consisting 2° is selected from the group consisting of a bond, of O, S, C(O), S(O), N(R⁴¹), and ON(R⁴¹); R2 18 Z0-0;

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 Z° is optionally $(CH\left(R^{11}\right))_{\bullet}-W^{22}-\left(CH\left(R^{42}\right)\right)_{h}$ wherein e and h are independently 0 or 1 and W^{22} is selected from the piperidinyl, 2,3-piperidinyl, 2,4-piperidinyl, 2,6cyclopentyl, 1,3-cyclopentyl, 2,3-morpholinyl, 2,4morpholinyl, 2,6-morpholinyl, 3,4-morpholinyl, 3,5morpholinyl, 1,2-piperazinyl, 1,3-piperazinyl, 2,3piperazinyl, 2,6-piperazinyl, 1,2-piperidinyl, 1,3piperidinyl, 3,4-piperidinyl, 1,2-pyrrolidinyl,1,3group consisting of CR*1=CR*2, 1,2-cyclopropyl, 1,2cyclobuty1, 1,2-cyclohexy1, 1,3-cyclohexy1, 1,2-

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pyridine ring and W22 is optionally substituted with one or more substituents selected from the group consisting of tetrahydrofuranyl, wherein 2° is directly bonded to the 2,4-tetrahydrofuranyl, 2,5-tetrahydrofuranyl, and 3,4pyrrolidinyl, 2,3-pyrrolidinyl, 2,4-pyrrolidinyl, 2,5pyrrolidinyl, 3,4-pyrrolidinyl, 2,3-tetrahydrofuranyl, R3, R10, R11, R12, and R13;

R'1 and R'2 are independently selected from the group consisting of hydrido, hydroxy, alkyl, and amino;

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optionally substituted by R3, the other carbon adjacent to substituted by \mathbb{R}^{12} , and any carbon adjacent to both \mathbb{R}^{10} and R^{12} is optionally substituted by $R^{11},\;$ with the proviso that substituted by \mathbb{R}^{10} , a carbon adjacent to \mathbb{R}^{13} and two atoms from the carbon at the point of attachment is optionally from the carbon at the point of attachment is optionally substituted by R11, a carbon adjacent to R' and two atoms Q is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to \mathbf{Z}^0 is the carbon at the point of attachment is optionally Q is other than a phenyl when Z° is a bond;

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 $\ensuremath{\mathbf{Q}}$ is optionally hydrido with the proviso that \mathbf{Z}^o is selected from other than a bond;

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consisting of hydrido, hydroxyalkyl, alkyl, alkoxyalkyl, K is CHR** wherein R** is selected from the group alkylthioalkyl, and haloalkyl;

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E° is selected from the group consisting of a bond, C(O)N(H), (H)NC(O), $(R^7)NS(O)_2$, and $S(O)_2N(R^7)$;

YAT IS Qb-Q";

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O' is (CR'R'), wherein b is an integer selected from 1 through 4, R17 is selected from the group consisting of the group consisting of hydrido, alkyl, haloalkyl, aroyl, and heteroarcyl with the proviso that there is at least hydrido, alkyl, and haloalkyl, and R^{10} is selected from one aroyl or heteroaroyl substituent, with the further proviso that no more than one aroyl or heteroaroyl is

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or a pharmaceutically acceptable salt thereof, wherein;

substituted by \mathbb{R}^{15} , and any carbon adjacent to both \mathbb{R}^{13} and substituted by R¹³, a carbon adjacent to R¹⁶ and two atoms from the carbon at the point of attachment is optionally substituted by R16, a carbon adjacent to R12 and two atoms from the carbon at the point of attachment is optionally B is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of optionally substituted by R^{12} , the other carbon adjacent to the carbon at the point of attachment is optionally attachment of said phenyl or heteroaryl ring to A is R^{15} is optionally substituted by R^{14} ;

 R^{12} , R^{33} , R^{34} , R^{35} , and R^{36} are independently selected hydroxyalkyl, carboalkoxy, carboxy, carboxamido, cyano, haloacetamido, amidino, guanidino, alkoxy, hydroxy, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy, from the group consisting of hydrido, acetamido, amino, alkoxyamino, alkylamino, alkylthio, and Ob;

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A is a bond or $(CH(\mathbb{R}^{15}))_{pa}-(W^7)_{pa}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W^{\prime} is

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R' is hydrido or alkyl;

R15 is selected from the group consisting of hydrido, halo, alkyl, and haloalkyl;

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R16, R17, R18, and R19 are independently selected from haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and the group consisting of hydrido, amidino, guanidino, than the one bonding said aroyl or said heteroaroyl; alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, alkoxyamino, alkylamino, alkylthio, alkylsulfinyl, carboxy, haloalkylthio, alkoxy, hydroxy, amino,

 $C(NR^{25})\,NR^{23}R^{24},$ with the proviso that $R^{16},\ R^{19},$ and \mathbb{Q}^{b} are not R16 or R19 is optionally selected from the group consisting of $NR^{20}R^{21},\ N\left(R^{26}\right)C\left(NR^{25}\right)N\left(R^{23}\right)\left(R^{24}\right),\ and$ simultaneously hydrido; cyano;

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hydrido, $N(R^{26}) C(NR^{25}) N(R^{23}) \left(R^{24}\right)$, and $C(NR^{25}) NR^{23} R^{24}$, with the from the group consisting of hydroxy, amino, alkylamino, from the group consisting of hydroxy, amino, alkylamino, \mathbb{Q}^b is selected from the group consisting of $NR^{10}R^{21},$ proviso that no more than one of \mathbb{R}^{20} and \mathbb{R}^{21} is selected and dialkylamino at the same time and with the further proviso that no more than one of \mathbb{R}^{23} and \mathbb{R}^{24} is selected and dialkylamino at the same time;

selected from the group consisting of hydrido, alkyl, $R^{20},\ R^{21},\ R^{23},\ R^{24},\ R^{25},$ and R^{26} are independently hydroxy, amino, alkylamino and dialkylamino.

In a most preferred embodiment of compounds of

Formula I, said compound is the formula:

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said heteroarcyl are bonded to the $CR^{37}R^{38}$ that is directly

further proviso that said aroyl and said heteroaroyl are

bonded to (CR37R38), at the same time, with the still

selected from the group consisting of Ris, Ri, Ris, and

optionally substituted with one or more substituents

R19, with another further proviso that said aroyl and

more than one alkyl or one haloalkyl is bonded to a ${
m CR}^{
m J}{
m R}^{
m 18}$

at the same time, and with the additional proviso that

said alkyl and haloalkyl are bonded to a carbon other

bonded to E°, with still another further proviso that no

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R¹ and X° are independently selected from the group consisting of hydrido, hydroxy, hydroxyamino, amidino, amino, cyano, hydroxyalkyl, alkoxy, alkyl, alkylamino, aminoalkyl, alkylthio, alkoxyamino, haloalkyl, and halo;

R2 is Z0-Q;

Z° is a bond;

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Q is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to 2° is optionally substituted by R³, the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R¹³, a carbon adjacent to R³ and two atoms from the carbon at the point of attachment is optionally substituted by R¹³, a carbon adjacent to R¹ and two atoms from the carbon at the point of attachment is optionally substituted by R¹³, and any carbon adjacent to both R¹³ and R¹³ is optionally substituted by R¹¹;

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R, R1, and R1 are independently selected from the group consisting of hydrido, hydroxy, amino, amidino, guanidino, alkylamino, alkylthio, alkoxy, alkylsulfinyl, alkylsulfonyl, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, carboxy, carboxamido, and cyano;

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R¹⁰ and R¹² are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkyl, alkoxy, alkoxyamino, hydroxy, amino, alkylsulfonamido, amidosulfonyl, hydroxyalkyl, aminoalkyl, halo, haloalkyl, carboalkoxy, carboxamido, carboxylkyl, and cyano;

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wherein one carbon of said phenyl or said heteroaryl is substituted by Q*, a carbon two or three atoms from the point of attachment of Q* to said phenyl or said heteroaryl is substituted by Q*, a carbon adjacent to the point of attachment of Q* is optionally substituted by R*;

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another carbon adjacent to the point of attachment of Q^* is optionally substituted by R^{16} , a carbon adjacent to Q^b is optionally substituted by R^{16} , and another carbon adjacent to Q^b is optionally substituted by R^{19} ;

R¹⁶, R¹⁷, R¹⁸, and R¹⁹ are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl,

haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano; R¹⁶ or R¹⁹ is optionally NR²⁰R²¹ or C(NR²⁸)NR²³R²⁴, with the proviso that R¹⁶, R¹⁹, and Q³ are not simultaneously hydrido;

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 \mathbb{Q}^b is selected from the group consisting of $NR^{13}R^{24},$ hydrido, and $C(NR^{25})NR^{24}R^{24},$ $R^{20},$ $R^{21},$ $R^{21},$ $R^{21},$ $R^{21},$ $R^{21},$ and R^{23} are independently hydrido or

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Q* is CH2.

In a further most preferred embodiment of compounds of Formula I, said compound is the formula:

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or a pharmaceutically acceptable salt thereof, wherein;

B is selected from the group consisting of hydrido, C2-C8 alkyl, C3-C8 alkenyl, C3-C8 alkynyl, and C2-C8 haloalkyl, wherein each member of group B is optionally substituted at any carbon up to and including 6 atoms from the point of attachment of B to A with one or more of the group consisting of R³³, R³⁴, R³⁴, and R³⁶;

R12, R13, R14, R15, and R16 are independently selected hydroxyalkyl, carboalkoxy, carboxy, carboxamido, cyano, haloacetamido, amidino, guanidino, alkoxy, hydroxy, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy, from the group consisting of hydrido, acetamido, amino, alkoxyamino, alkylamino, alkylthio, and Qb;

A is a bond or $(CH(\mathbb{R}^{15}))_{ps}$ - $(W^7)_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W' is N(R');

R' is hydrido or alkyl;

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R15 is selected from the group consisting of hydrido, halo, alkyl, and haloalkyl;

R' and X° are independently selected from the group consisting of hydrido, hydroxy, hydroxyamino, amidino, amino, cyano, hydroxyalkyl, alkoxy, alkyl, alkylamino, aminoalkyl, alkylthio, alkoxyamino, haloalkyl,

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haloalkoxy, and halo;

R2 18 Z0-Q;

Z° is a bond;

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optionally substituted by \mathbb{R}^9 , the other carbon adjacent to substituted by R^{12} , and any carbon adjacent to both R^{10} and from the carbon at the point of attachment is optionally substituted by R10, a carbon adjacent to R13 and two atoms from the carbon at the point of attachment is optionally Q is phenyl or a heteroaryl of 5 or 6 ring members, substituted by R13, a carbon adjacent to R3 and two atoms wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to \mathbf{Z}^0 is the carbon at the point of attachment is optionally R12 is optionally substituted by R11;

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R, R11, and R13 are independently selected from the guanidino, alkylamino, alkylthio, alkoxy, alkylsulfinyl, alkylsulfonyl, amidosulfonyl, alkyl, halo, haloalkyl, group consisting of hydrido, hydroxy, amino, amidino,

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haloalkoxy, hydroxyalkyl, carboxy, carboxamido, and

R10 and R12 are independently selected from the group amidino, guanidino, alkyl, alkoxy, alkoxyamino, hydroxy, hydroxyalkyl, aminoalkyl, halo, haloalkyl, carboalkoxy, amino, alkylamino, alkylsulfonamido, amidosulfonyl. consisting of hydrido, acetamido, haloacetamido, carboxy, carboxamido, carboxyalkyl, and cyano;

point of attachment of \mathbb{Q}^{ullet} is optionally substituted by $\mathbb{R}^{17},$ heteroaryl is substituted by Qb, a carbon adjacent to the is optionally substituted by $R^{1\theta},\ a\ carbon\ adjacent\ to\ Q^b$ another carbon adjacent to the point of attachment of Q* Y° is phenyl or a heteroaryl of 5 or 6 ring members, substituted by Q*, a carbon two or three atoms from the wherein one carbon of said phenyl or said heteroaryl is is optionally substituted by R¹⁶, and another carbon point of attachment of Q to said phenyl or said adjacent to \mathbb{Q}^b is optionally substituted by \mathbb{R}^{19} ;

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R16, R17, R18, and R19 are independently selected from the group consisting of hydrido, amidino, guanidino, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano; carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl,

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 $C(NR^{25})NR^{23}R^{24}$, with the proviso that R^{16} , R^{19} , and Q^{3} are not R16 or R19 is optionally selected from the group consisting of NR20R21, N(R26)C(NR25)N(R21)(R24), and simultaneously hydrido;

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R20, R21, R21, R24, R25, and R26 are independently hydrido \mathbb{Q}^{b} is selected from the group consisting of $NR^{20}R^{21}$, hydrido, $N(R^{26})C(NR^{25})N(R^{23})$ (R^{24}) , and $C(NR^{25})NR^{23}R^{24}$,

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O is CH3.

compounds of Formula I, said compound is the formula; In a still further most preferred embodiment of

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atoms from the point of attachment and adjacent to the \mathbb{R}^{13} carbon at the point of attachment of B to A is optionally carbons and a nitrogen adjacent to the carbon atom at the point of attachment are optionally substituted with R9 or R13, a ring carbon or nitrogen adjacent to the R9 position substituted with oxo provided that no more than one ring attachment and adjacent to the R10 position is optionally and two atoms from the point of attachment is optionally substituted with R^{10} , a ring carbon or nitrogen adjacent or a pharmaceutically acceptable salt thereof, wherein; substituted with R¹³, a ring carbon other than the ring attachment is optionally substituted with R12, a ring substituted with R11, a ring carbon or nitrogen three attachment and adjacent to the R11 and R13 positions is heterocyclyl, wherein each ring carbon is optionally carbon is substituted by oxo at the same time, ring to the R¹³ position and two atoms from the point of B is a C3-C7 cycloalkyl or a C4-C6 saturated carbon or nitrogen three atoms from the point of position is optionally substituted with R33, and carbon or nitrogen four atoms from the point of optionally substituted with R14;

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R3, R11, and R13 are independently selected from the guanidino, alkylamino, alkylthio, alkoxy, alkylsulfinyl, group consisting of hydrido, hydroxy, amino, amidino, alkylsulfonyl, amidosulfonyl, alkyl, halo, haloalkyl,

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haloalkoxy, hydroxyalkyl, carboxy, carboxamido, and

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cyano;

 \mathbb{R}^{10} and \mathbb{R}^{12} are independently selected from the group

amidino, guanidino, alkyl, alkoxy, alkoxyamino, hydroxy, hydroxyalkyl, aminoalkyl, halo, haloalkyl, carboalkoxy, amino, alkylamino, alkylsulfonamido, amidosulfonyl, consisting of hydrido, acetamido, haloacetamido, carboxy, carboxamido, carboxyalkyl, and cyano;

R13 and R34 are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, alkylamino, alkylthio, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, carboalkoxy, guanidino, alkoxy, hydroxy, amino, alkoxyamino,

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carboxy, carboxamido, and cyano; R33 is optionally Qb;

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A is a bond or $(CH(R^{15}))_{pa} - (W^2)_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W^{1} is N(R');

R' is hydrido or alkyl;

R15 is selected from the group consisting of hydrido, 20

halo, alkyl, and haloalkyl;

R' and X' are independently selected from the group consisting of hydrido, hydroxy, hydroxyamino, amidino, amino, cyano, hydroxyalkyl, alkoxy, alkyl, alkylamino, aminoalkyl, alkylthio, alkoxyamino, haloalkyl,

haloalkoxy, and halo; 25

R2 is Z0-Q;

Z° is a bond;

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optionally substituted by R', the other carbon adjacent to substituted by R10, a carbon adjacent to R13 and two atoms from the carbon at the point of attachment is optionally substituted by R13, a carbon adjacent to R9 and two atoms Q is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to \mathbf{z}^{o} is the carbon at the point of attachment is optionally

from the carbon at the point of attachment is optionally substituted by R^{12} , and any carbon adjacent to both R^{10} and R^{1} is optionally substituted by R^{11} ;

 Y^o is phenyl or a heteroaryl of 5 or 6 ring members, wherein one carbon of said phenyl or said heteroaryl is substituted by Q^s , a carbon two or three atoms from the point of attachment of Q^s to said phenyl or said heteroaryl is substituted by Q^b , a carbon adjacent to the point of attachment of Q^s is optionally substituted by R^{19} , another carbon adjacent to the point of attachment of Q^s is optionally substituted by R^{18} , a carbon adjacent to Q^s is optionally substituted by R^{18} , and another carbon adjacent to Q^b is optionally substituted by R^{18} , and another carbon adjacent to Q^b is optionally substituted by R^{19} ,

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R¹⁴, R¹³, and R¹⁹ are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano; R¹⁶ or R¹⁹ is optionally NR²⁰R²¹ or C(NR²³)NR²³R²³, with

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 R^{16} or R^{19} is optionally $NR^{20}R^{21}$ or $C\left(NR^{29}\right)NR^{21}R^{24}$, with the proviso that $R^{16},\ R^{19},\ and\ Q^{0}$ are not simultaneously hydrido;

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 Q^{b} is selected from the group consisting of $NR^{20}R^{21},$ hydrido, and $C(NR^{25})NR^{23}R^{24},$

 $R^{20},\ R^{21},\ R^{21},\ R^{24},$ and R^{35} are independently hydrido or alkyl;

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Q* is CH2.

In a preferred specific embodiment of Formula I, compounds have the formula:

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or a pharmaceutically acceptable salt thereof, wherein, M is N or $N\!\!\to\!\!0$,

substituted by R³⁵, and any carbon adjacent to both R³³ and yl, and 1,2,3-triazin-5-yl,, wherein a carbon adjacent to pyrazolyl, 1,2,4-triazol-3-yl, 1,2,4-triazol-5-yl, 1,2,4yl, 1,3,4-oxadiazol-5-yl, 3-isothiazolyl, 5-isothiazolyl, pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, substituted by R16, a carbon adjacent to R12 and two atoms oxadiazol-3-yl, 1,2,4-oxadiazol-5-yl, 1,3,4-oxadiazol-3-1,2,4-triazin-5-yl, 1,2;4-triazin-6-yl, 1,2,3-triazin-4from the carbon at the point of attachment is optionally substituted by R13, a carbon adjacent to R16 and two atoms from the carbon at the point of attachment is optionally 2-oxazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 2-B is selected from the group consisting of phenyl, 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3-4-pyridazinyl, 1,3,5-triazin-2-yl, 1,2,4-triazin-3-yl, pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-pyrazolyl, 4the carbon at the point of attachment is optionally substituted by R12, the other carbon adjacent to the carbon at the point of attachment is optionally pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-R15 is optionally substituted by R14; 20 ហ 50 15

R13, R13, R14, R15, and R16 are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, methyl, ethyl, isopropyl, propyl, methoxy, ethoxy, isopropoxy, propoxy, hydroxy, amino, methoxyamino, ethoxyamino, acteamido, trifluoroacetamido, nitro, aminomethyl, 1-aminoethyl, 2-aminoethyl, N-methylamino, dimethylamino, N-ethylamino, methylthio, ethylthio, isopropylthio, trifluoromethylthio, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3-pentafluoropropyl, trifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, chloro, bromo, amidosulfonyl, N-methylamidosulfonyl, N.N-dimethylamidosulfonyl, propanoyl,

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trifluoroacetyl, pentafluoropropanoyl, hydroxymethyl, 1-hydroxyethyl, 2,2,2-trifluoro-1-hydroxyethyl, 2,2,2-trifluoro-1-hydroxyethyl, 2,2,2-trifluoromethyl-1-hydroxyethyl, carboxymethyl, methoxycarbonyl, ethoxycarbonyl, amidocarbonyl, N-methylamidocarbonyl, N-dimethylamidocarbonyl, cyano, and Q^b;

methyl-3-pentynyl, 3-hexyl, 1-ethyl-2-butenyl, 1-ethyl-3methyl-2-hexynyl, 1-methyl-3-hexynyl, 1-methyl-4-hexynyl, ethyl-4-pentenyl, 1-butyl-2-propenyl, 1-ethyl-2-pentynyl, propenyl, 2-methylbutyl, 2-methyl-2-butenyl, 2-methyl-3octenyl, 5-octenyl, 6-octenyl, 7-octenyl, 2-octynyl, 3-B is selected from the group consisting of hydrido, butyl, tert-butyl, isobutyl, 2-methylpropenyl, 1-pentyl, butenyl, 2-methyl-3-butynyl, 3-methylbutyl, 3-methyl-2hexenyl, 4-hexenyl, 5-hexenyl, 2-hexynyl, 3-hexynyl, 4isopropyl, butyl, 2-butenyl, 3-butenyl, 2-butynyl, secheptyl, 2-heptenyl, 3-heptenyl, 4-heptenyl, 5-heptenyl, heptenyl, 1-methyl-5-heptenyl, 1-methyl-6-heptenyl, 1pentenyl, 1-methyl-4-pentenyl, 1-methyl-2-pentynyl, 1heptenyl, 1-methyl-5-heptenyl, 1-methyl-6-heptenyl, 1trimethylsilyl, ethyl, 2-propenyl, 2-propynyl, propyl, 1-ethyl-3-pentynyl, 1-octyl, 2-octenyl, 3-octenyl, 4-3-heptyl, 1-ethyl-2-pentenyl, 1-ethyl-3-pentenyl, 1octynyl, 4-octynyl, 5-octynyl,6-octynyl, 2-octyl, 1butenyl, 3-methyl-3-butenyl, 1-hexyl, 2-hexenyl, 3methyl-2-heptenyl, 1-methyl-3-heptenyl, 1-methyl-4methyl-2-heptynyl, 1-methyl-3-heptynyl, 1-methyl-4methyl-2-heptenyl, 1-methyl-3-heptynyl, 1-methyl-4heptynyl, 2-heptyl, 1-methyl-2-hexenyl, 1-methyl-3pentynyl, 2-pentyl, 1-methyl-2-butenyl, 1-methyl-3butenyl, 1-propyl-2-propenyl, 1-ethyl-2-butynyl, 1hexenyl, 1-methyl-4-hexenyl, 1-methyl-5-hexenyl, 1-2-hexyl, 1-methyl-2-pentenyl, 1-methyl-3-6-heptenyl, 2-heptynyl, 3-heptynyl, 4-heptynyl, 5-2-pentenyl, 3-pentenyl, 4-pentenyl, 2-pentynyl, 3butenyl, 1-methyl-2-butynyl, 3-pentyl, 1-ethyl-2hexynyl,

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the point of attachment is optionally substituted with R° cycloheptyl, cyclooctyl, 2-morpholinyl, 3-morpholinyl, 4morpholinyl, 1-piperazinyl, 2-piperazinyl, 1-piperidinyl, pyrrolidinyl, 2-pyrrolidinyl, 3-pyrrolidinyl, 2-dioxanyl, hexynyl, 1-ethyl-3-hexynyl, 1-ethyl-4-hexynyl, 1-ethyl-5-4H-2-pyranyl, 4H-3-pyranyl, 4H-4-pyranyl, 4H-pyran-4-onecarbon and nitrogen atoms adjacent to the carbon atom at hexenyl, 1-ethyl-3-hexenyl, 1-ethyl-4-hexenyl, 1-ethyl-2or R^{13} , a ring carbon or nitrogen atom adjacent to the R^{9} at any carbon up to and including 5 atoms from the point B is optionally selected from the group consisting setrahydrothienyl, and 3-tetrahydrothienyl, wherein each wherein each member of group B is optionally substituted azetidin-1-yl, azetidin-2-yl, azetidin-3-yl, thiaetan-2nitrogen atom adjacent to the R13 position and two atoms oxabicyclo[2.2.1]heptan-2-yl, bicyclo[3.1.0]hexan-6-yl, position and two atoms from the point of attachment is pentenyl, 1-propyl-3-pentenyl, 1-propyl-4-pentenyl, 1pentynyl, 1-butyl-2-butynyl, 1-butyl-3-butenyl, 2,2,2trifluoroethyl, 2,2-difluoropropyl, 4-trifluoromethyl-5,5,6,6,6-pentafluorohexyl, and 3,3,3-trifluoropropyl, yl, thiaetan-3-yl, cyclopentyl, cyclohexyl, adamantyl, ring carbon is optionally substituted with R¹³, a ring of attachment of B to A with one or more of the group of cyclopropyl, cyclobutyl, oxetan-2-yl, oxetan-3-yl, optionally substituted with R10, and a ring carbon or 2-yl, 4H-pyran-4-one-3-yl, 2-tetrahydrofuranyl, 3hexenyl, 1-pentyl-2-propenyl, 4-octyl, 1-propyl-2neptynyl, 1-methyl-5-heptynyl, 3-octyl, 1-ethyl-2butyl-2-butenyl, 1-propyl-2-pentynyl, 1-propyl-3-2-piperidinyl, 3-piperidinyl, 4-piperidinyl, 1-5,5,5-trifluoropentyl, 4-trifluoromethylpentyl, etrahydrofuranyl, 2-tetrahydropyranyl, 3tetrahydropyranyl, 4-tetrahydropyranyl, 2norbornyl, 3-trifluoromethylnorbornyl, 7consisting of R12, R11, R14, R15, and R16; 20 25 30 35 ហ 10 12

ź phenylethyl)amidocarbonyl, N-benzylamidosulfonyl, N-(2methanesulfonamido, amidosulfonyl, N-methylamidosulfonyl, N, N-dimethylamidosulfonyl, hydroxymethyl, 1-hydroxyethyl from the group consisting of hydrido, amidino, guanidino carboxy, carboxymethyl, methyl, ethyl, propyl, isopropyl cyclobutylamidocarbonyl, N-cyclopentylamidocarbonyl, Naminoethyl, N-methylamino, dimethylamino, N-ethylamino, $R^9,\ R^{10},\ R^{11},\ R^{12},\ and\ R^{13}$ are independently selected cyclohexylamidocarbonyl, fluoro, chloro, bromo, cyano, >oenzylamidocarbonyl, N-(2-chlorobenzyl)amidocarbonyl, methoxy, ethoxy, isopropoxy, propoxy, hydroxy, amino, chlorobenzyl) amidosulfonyl, N-ethylamidocarbonyl, Nsobutylamidocarbonyl, N-(2-butyl)amidocarbonyl, Nmethoxycarbonyl, ethoxycarbonyl, amidocarbonyl, Nmethylamidocarbonyl, N,N-dimethylamidocarbonyl, Ntrifluoroacetamido, aminomethyl, 1-aminoethyl, 2sopropylamidocarbonyl, N-propylamidocarbonyl, Ncyclobutoxy, cyclohexoxy, cyclohexylmethoxy, 4-2-hydroxyethyl, 2,2,2-trifluoro-1-hydroxyethyl, :rifluoromethylbenzyl) amidocarbonyl, N-(1phenylethyl)amidocarbonyl, N-(1-methyl-1methoxyamino, ethoxyamino, acetamido, (3-fluorobenzyl)amidocarbonyl, N-(2-

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crifluoromethycyclohexylmethoxy, cyclopentoxy, benzyl, senzyloxy, 4-bromo-3-fluorophenoxy, 3-bromobenzyloxy, ylmethylamino, 4-butoxyphenamino, 3-chlorobenzyl, 4bromobenzyloxy, 4-bromobenzylamino, 5-bromopyrid-2chlorophenoxy, 4-chloro-3-ethylphenoxy, 4-chloro-3ethylbenzylamino, 4-chloro-3-ethylphenylamino, 3chlorophenylaulfonyl, 5-chloropyrid-3-yloxy, 2cyanopyrid-3-yloxy, 2,3-difluorobenzyloxy, 2,4difluorobenzyloxy, 3,4-difluorobenzyloxy, 2,5chlorobenzylsulfonyl, 4-chlorophenylamino, 4chlorobenzyloxy, 4-chlorobenzyloxy, 4-

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3-trifluoromethoxyphenoxy, 4-trifluoromethoxyphenoxy, 3trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, dimethylbenzyloxy, 4-ethoxyphenoxy, 4-ethylbenzyloxy, 3methylphenoxy, 4-isopropylbenzyloxy, 3-isopropylphenoxy, trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3trifluoromethylthiobenzyloxy, 2,3,4-trifluorophenoxy, 2,3,5-trifluorophenoxy, 3-pentafluoroethylphenoxy, 3trifluoromethylbenzyloxy, 4-trifluoromethylbenzyloxy, fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2isopropylphenoxy, 4-isopropylphenoxy, 4-isopropyl-3difluorobenzyloxy, 4-difluoromethoxybenzyloxy, 2,3fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4phenylethyl, 2-phenylethylamino, phenylsulfonyl, 4-isopropylphenoxy, 4-isopropyl-3-methylphenoxy, trifluoromethylphenoxy, 4-isopropylbenzyloxy, 3phenylamino, 1-phenylethoxy, 2-phenylethoxy, 2trifluoromethylbenzyloxy, 2-fluorophenoxy, 4ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5methylphenoxy, 4-fluorobenzyloxy, 2-fluoro-3dimethylphenoxy, 3,4-dimethylbenzyloxy, 3,5difluorobenzyloxy, 3,5-difluorophenoxy, 3,5difluorophenoxy, 2,4-difluorophenoxy, 2,5difluorophenoxy, 3,5-dimethylphenoxy, 3,4-(1,1,2,2-tetrafluoroethoxy)phenoxy, and3trifluoromethylbenzyloxy, 4-fluoro-2trifluoromethylbenzyloxy, 3-fluoro-5trifluoromethylbenzyloxy, 4-fluoro-3-2,4-bis-trifluoromethylbenzyloxy, 3trifluoromethylthiobenzyloxy, 4-30 20 25 15 2

0, S, NH, N(CH3), N(OH), C(O), CH2, CH3CH, CF3CH, NHC(O), A is selected from the group consisting of a bond, C(0) CCF3, CH2C(0), (0) CCH2, CH2CH2, CH3CH3CH2, CH3CHCH2, $N(CH_3)C(0)$, C(0)NH, $C(0)N(CH_3)$, $CF_3CC(0)$, $C(0)CCH_3$, trifluoromethylthiophenoxy;

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 CF_3CHCH_3 , $CH_3CC(0)CH_2$, $CF_3CC(0)CH_2$, $CH2C(0)CCH_3$, $CH_2C(0)CCF_3$, $CH_3CH_2C(0)$, and $CH_3(0)CCH_2$;

A is optionally selected from the group consisting of CH,N(CH,), CH,N(CH,CH,), CH,CH,N(CH,CH,), and CH,CH,N(CH,CH,CH,the proviso that B is hydrido;

Ja is independently selected from the group consisting of N and $C \cdot X^{\sigma}$;

Jb is independently selected from the group

consisting of N and C-R¹,

Jc is independently selected from the group
consisting of N and C-R², with the proviso that at least
one of Ja, Jb, and Jc are not a nitrogen(N).

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R¹ and X° are independently selected from the group consisting of hydrido, hydroxy, amino, thiol, amidino, hydroxyamino, aminomethyl, 1-aminoethyl, 2-aminoethyl, septylamino, dimethylamino, cyano, methyl, ethyl, isopropyl, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3-pentafluoropropyl, methoxy, ethoxy, propoxy, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, methoxyamino, ethoxyamino, methylthio, ethylthio, trifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, chloro, and bromo;

R is Z°-Q;

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Q is selected from the group consisting of phenyl, 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3-pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-pyrazolyl, 4-pyrazolyl, 1,2,4-triazol-3-yl, 1,2,4-triazol-5-yl, 1,3,4-oxadiazol-3-yl, 1,3,4-oxadiazol-5-yl, 1,3,4-oxadiazol-3-yl, 1,3,4-oxadiazol-5-yl, 3-isothiazolyl, 2-oxazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isothiazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-pyrimidinyl, 4-pyrimidinyl, 3-pyrimidinyl, 3-pyrimidinyl, 3-pyrimidinyl, 3-pyrimidinyl,

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4-pyridazinyl, 1,3,5-triazin-2-yl, 1,2,4-triazin-3-yl, 1,2,4-triazin-5-yl, 1,2,4-triazin-6-yl, 1,2,3-triazin-4-yl, and 1,2,3-triazin-5-yl, wherein a carbon adjacent to the carbon at the point of attachment is optionally substituted by R³, the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R³, a carbon adjacent to R³ and two atoms from the carbon at the point of attachment is optionally substituted by R³, a carbon adjacent to R³ and two atoms from the carbon at the point of attachment is optionally substituted by R³, and any carbon adjacent to both R³ and R³ is optionally substituted by R³; and any carbon adjacent to both R³ and R³ is

K is CR*R*b wherein R** and R*b are independently selected from the group consisting of methyl, ethyl, propyl, isopropyl, fluoro, chloro, hydroxy, hydroxymethyl, 1-hydroxyethyl, methoxymethyl, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoromethyl, methylthiomethyl, and hydrido;

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 E^o is a bond, $C(O)\,N\,(H)\,,$ $(H)\,NC\,(O)\,,$ and $S\,(O)\,{}_2N\,(H)\,;$ Y^o is selected from the group of formulas consisting

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1-Qb-4-Q*-2-R14-3-R17-5-R18-6-R19benzene,

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3-Qb-6-Q-2-R18-5-R18-4-R19pyridazine,

2-Qb-5-Q"-6-R17-4-R18-3-R19pyridine,

 $2-Q^{b}-5-Q^{a}-4-R^{17}-6-R^{18}pyrimidine,$

3-Q^b-6-Q^e-2-R¹⁶-5-R¹⁸-4-R¹⁹pyridine,

5-Qb-2-Q-4-R16-6-R19pyrimidine,

2-Qb-5-Q"-3-R16-6-R18pyrazine,

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3-0b-5-Q"-4-R16-2-R19pyrrole,

3-Q^b-5-Q"-4-R¹⁶-2-R¹⁹thiophene,

2-Qb-5-Q-3-R16-4-R17thiophene,

3-0°-5-0°-4-R16-2-R19furan,

2-Qb-5-Q*-3-R16-4-R17pyrrole,

4-Qb-2-Q6-5-R19imidazole,

2-Q^-4-Q"-5-R17imidazole,

2-Qb-5-Q-3-R16-4-R17furan,

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2-Qb-5-Q*-4-R17thiazole;

Ris, Ri7, Ris, and Ris are independently selected from the group consisting of hydrido, methyl, ethyl, isopropyl, amidino, guanidino, carboxy, methoxy, ethoxy, isopropoxy, propoxy, hydroxy, amino, methoxyamino, ethoxyamino, aminomethyl, 1-aminoethyl, 2-aminoethyl, N-N-methylamino, dimethylamino, N-ethylamino, methylthio, ethylthio, isopropylthio,

trifluoromethylthio, methylsulfinyl, ethylsulfinyl, methylsulfonyl, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3-pentafluoropropyl, trifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, chloro, bromo, amidosulfonyl, N-methylamidosulfonyl, N-dimethylamidosulfonyl, acetyl, propanoyl, trifluoroacetyl, pentafluoropropanoyl,

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hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, and cyano; Q² is selected from the group consisting of NR²⁸R, hydrido, C(NR²³)NR²³R²⁴ and N(R²⁴)C(NR²⁵)N(R²³) (R²⁴), with the proviso that no more than one of R²⁰ and R²¹ is hydroxy, N-methylamino, and N,N-dimethylamino at the same time and that no more than one of R²³ and R²⁴ is hydroxy, N-methylamino, and N,N-dimethylamino at the same time;

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R20, R21, R21, R24, R25, and R26 are independently selected from the group consisting of hydrido, methyl, ethyl, propyl, butyl, isopropyl, hydroxy, 2-aminoethyl, 2-(N-methylamino)ethyl, and 2-(N,N-dimethylamino)ethyl;

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Q' is selected from the group consisting of a bond, CH₂, CH₂CH₂, CH₃CH, CF₃CHCH₂, CF₃CHCH₃, CH₃(CH₃)CH, CH=CHCH₂, CF=CHCH₃, C(CH₃)=CHCH₃, CH₃CHCH₃, CH₃CHCH₃, CH₃CH₃CHCH₃, CH₃CH₃CHCH₃, CH₃CH₃CHCH₃, CH₃CH₃CHCH₃, CH₃CC(CH₃)=CHCH₃, CH₃CHCH₃, CH₃CHCH₃, and CH₃C(CH₃)=CHCH₃CH₃.

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In a more preferred specific embodiment of Formula's, compounds have the formula:

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3-Qb-5-Q-4-Risoxazole,

5-Qb-3-Q*-4-R161soxazole,

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2-Q^b-5-Q^e-4-R¹⁶pyrazole,

 $4-Q^{b}-2-Q^{e}-5-R^{19}$ thiazole, and

1-pyridazinyl, and 1,3,5-triazin-2-yl, wherein a carbon or a pharmaceutically acceptable salt thereof, wherein; B is selected from the group consisting of phenyl, 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3pyrazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 2pyrroly1, 2-imidazoly1, 4-imidazoly1, 3-pyrazoly1, 4pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-

carbon adjacent to R32 and two atoms from the carbon at the carbon adjacent to R^{36} and two atoms from the carbon at the adjacent to the carbon at the point of attachment, of said pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, point of attachment is optionally substituted by \mathbb{R}^{35} , and phenyl or heteroaryl ring to A is optionally substituted point of attachment is optionally substituted by R^{13} , a point of attachment is optionally substituted by $R^{36},\ a$ by \mathbb{R}^{12} , the other carbon adjacent to the carbon at the ny carbon adjacent to both R^{33} and R^{35} is optionally substituted by R34;

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from the group consisting of hydrido, amidino, guanidino, trifluoromethy1, pentafluoroethy1, 2,2,2-trifluoroethy1, tetrafluoroethoxy, fluoro, chloro, bromo, amidosulfonyl, $R^{32},\ R^{33},\ R^{34},\ R^{35},$ and R^{36} are independently selected 2,2,3,3,3-pentafluoropropyl, trifluoromethoxy, 1,1,2,2sarboxy, methoxy, ethoxy, isopropoxy, propoxy, hydroxy, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 2,2,2crifluoroacetamido, N-methylamino, dimethylamino, N-N-methylamidosulfonyl, N,N-dimethylamidosulfonyl, ethylamino, methylthio, ethylthio, isopropylthio, amino, methoxyamino, ethoxyamino, acetamido,

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ethoxycarbonyl, amidocarbonyl, N-methylamidocarbonyl, trifluoro-1-hydroxyethyl, methoxycarbonyl, N, N-dimethylamidocarbonyl, cyano, and $\mathbb{Q}^{\flat};$

NH, N(CH3), N(OH), CH2, CH3CH, CF3CH, NHC(O), N(CH3)C(O), A is selected from the group consisting of a bond, C(0)NH, C(0)N(CH3), CH2CH2, CH2CH2CH2, CH3CHCH2, and CF, CHCH,

 R^{16} , R^{17} , R^{19} , and R^{19} are independently selected from ethoxy, isopropoxy, propoxy, hydroxy, amino, aminomethyl, 1-aminoethyl, 2-aminoethyl, N-methylamino, dimethylamino, isopropyl, propyl, carboxy, amidino, guanidino, methoxy, tetrafluoroethoxy, fluoro, chloro, bromo, hydroxymethyl, N-ethylamino, methylthio, ethylthio, isopropylthio, trifluoromethylthio, methylsulfinyl, ethylsulfinyl, pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3the group consisting of hydrido, methyl, ethyl, methylsulfonyl, ethylsulfonyl, trifluoromethyl, pentafluoropropyl, trifluoromethoxy, 1,1,2,2-

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R16 or R19 is optionally C(NR25)NR23R24 with the proviso that R16, R19, and Qb are not simultaneously hydrido; 1-hydroxyethyl, 2-hydroxyethyl, and cyano;

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Qb is C(NR²⁵)NR²³R²⁴ or hydrido, with the proviso that no more than one of R23 and R24 is hydroxy at the same time;

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R11, R24, and R25 are independently selected from the group consisting of hydrido, methyl, ethyl, and hydroxy. In another more preferred specific embodiment of Formula I, compounds have the formula:

or a pharmaceutically acceptable salt thereof, wherein;

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3-methylbutyl, 3-methyl-2-butenyl, 3-methyl-3-butenyl, 1methy1-2-buteny1, 2-methy1-3-buteny1, 2-methy1-3-butyny1, butynyl, 3-pentyl, 1-ethyl-2-propenyl, 2-methylbutyl, 2-B is selected from the group consisting of hydrido, ethyl, 2-propynyl, 2-propenyl, propyl, isopropyl, butyl, 2-butenyl, 3-butenyl, 2-butynyl, sec-butyl, tert-butyl, pentenyl, 4-pentenyl, 2-pentynyl, 3-pentynyl, 2-pentyl, hexyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 5-hexenyl, 2isobutyl, 2-methylpropenyl, 1-pentyl, 2-pentenyl, 3-1-methyl-2-butenyl, 1-methyl-3-butenyl, 1-methyl-2hexynyl, 3-hexynyl, 4-hexynyl, 2-hexyl, 1-methyl-2-

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methyl-2-pentynyl, 1-methyl-3-pentynyl, 3-hexyl, 1-ethylmethyl-3-hexenyl, 1-methyl-4-hexenyl, 1-methyl-5-hexenyl, heptenyl, 5-heptenyl, 6-heptenyl, 2-heptynyl, 3-heptynyl, 4-heptynyl, 5-heptynyl, 2-heptyl, 1-methyl-2-hexenyl, 1wherein each member of group B is optionally substituted pentenyl, 1-methyl-3-pentenyl, 1-methyl-4-pentenyl, 1trifluoroethyl, 2,2-difluoropropyl, 4-trifluoromethyl-5,5,6,6,6-pentafluorohexyl, and 3,3,3-trifluoropropyl, 2-butenyl, 1-ethyl-3-butenyl, 1-propyl-2-propenyl, 1ethyl-2-butynyl, 1-heptyl, 2-heptenyl, 3-heptenyl, 4pentenyl, 1-ethyl-4-pentenyl, 1-butyl-2-propenyl, 1-1-methyl-2-hexynyl, 1-methyl-3-hexynyl, 1-methyl-4hexynyl, 3-heptyl, 1-ethyl-2-pentenyl, 1-ethyl-3-5,5,5-trifluoropentyl, 4-trifluoromethylpentyl, ethyl-2-pentynyl, 1-ethyl-3-pentynyl, 2,2,2-

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from the group consisting of hydrido, amidino, guanidino, R12, R13, R34, R35, and R36 are independently selected trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, carboxy, methoxy, ethoxy, isopropoxy, propoxy, hydroxy, trifluoroacetamido, N-methylamino, dimethylamino, Nethylamino, methylthio, ethylthio, isopropylthio, amino, methoxyamino, ethoxyamino, acetamido,

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at any carbon up to and including 5 atoms from the point

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of attachment of B to A with one or more of the group

consisting of R12, R13, R34, R15, and R16;

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tetrafluoroethoxy, fluoro, chloro, bromo, amidosulfonyl, 2,2,3,3,3-pentafluoropropyl, trifluoromethoxy, 1,1,2,2hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 2,2,2ethoxycarbonyl, amidocarbonyl, N-methylamidocarbonyl, N-methylamidosulfonyl, N,N-dimethylamidosulfonyl, trifluoro-1-hydroxyethyl, methoxycarbonyl, $N,N-dimethylamidocarbonyl,\ cyano,\ and\ Q^b;$ A is selected from the group consisting of bond, NH, $N(CH_3)$, N(OH), CH_2 , CH_3CH , CF_3CH , NHC(O), $N(CH_3)C(O)$, C(0)NH, C(0)N(CH3), CH2CH3, CH2CH2CH2, CH3CHCH2, and

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1-aminoethyl, 2-aminoethyl, N-methylamino, dimethylamino, ethoxy, isopropoxy, propoxy, hydroxy, amino, aminomethyl, isopropyl, propyl, carboxy, amidino, guanidino, methoxy, R16, R17, R18, and R19 are independently selected from trifluoromethylthio, methylsulfinyl, ethylsulfinyl, N-ethylamino, methylthio, ethylthio, isopropylthio, pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3the group consisting of hydrido, methyl, ethyl, methylaulfonyl, ethylaulfonyl, trifluoromethyl, CF,CHCH2;

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tetrafluoroethoxy, fluoro, chloro, bromo, hydroxymethyl, pentafluoropropyl, trifluoromethoxy, 1,1,2,2-1-hydroxyethyl, 2-hydroxyethyl, and cyano;

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N(R26)C(NR28)N(R29)(R24), with the proviso that R16, R19, and R16 or R19 is optionally selected from the group consisting of NR20R21, C(NR25)NR21R24, and Q are not simultaneously hydrido;

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hydrido, $C(NR^{25})NR^{23}R^{24}$, and $N(R^{26})C(NR^{25})N(R^{23})$ (R^{24}), with the proviso that no more than one of \mathbb{R}^{20} and \mathbb{R}^{21} is hydroxy at the same time and with the further proviso that no more \mathbb{Q}^{\flat} is selected from the group consisting of $NR^{20}R^{21},$ than one of R23 and R24 is hydroxy at the same time;

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selected from the group consisting of hydrido, methyl, $R^{20},\ R^{21},\ R^{23},\ R^{24},\ R^{25},$ and R^{26} are independently ethyl, propyl, butyl, isopropyl, and hydroxy.

In still another more preferred specific embodiment of Formula I, compounds have the formula:

or a pharmaceutically acceptable salt thereof, wherein;

B is selected from the group consisting of cyclopropyl, cyclobutyl, oxetan-3-yl, azetidin-1-yl, azetidin-2-yl, azetidin-3-yl, thiaetan-3-yl, cyclopentyl, cyclohexyl, norbornyl, 7-oxabicyclo[2.2.1]heptan-2-yl, bicyclo[3.1.0]hexan-6-yl, cycloheptyl, 2-morpholinyl, 4-morpholinyl, 1-piperazinyl, 2-piperazinyl, 2-piperidinyl, 2-piperidinyl, 3-piperidinyl, 3-pyrrolidinyl, 4H-2-pyranyl, 4H-3-pyranyl, 4H-3-pyranyl, 4H-3-pyranyl, 4-yyranyl, 3-tetrahydrofuranyl, 3-tetrahydrofuranyl, 3-tetrahydropyranyl, 3-tetrahydropyranyl, 4-tetrahydropyranyl, 2-tetrahydropyranyl, 3-tetrahydrothienyl, and 3-tetrahydrothienyl, wherein each ring carbon is optionally substituted with R³¹, ring carbons and a nitrogen adjacent to the carbon atom at the point of attachment are

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tetrahydropyranyl, 3-tetrahydropyranyl, 4tetrahydropyranyl, 2-tetrahydrothienyl, and 3tetrahydrothienyl, wherein each ring carbon is optionally
substituted with R¹³, ring carbons and a nitrogen adjacent
to the carbon atom at the point of attachment are
optionally substituted with R³ or R¹³, a ring carbon or
nitrogen adjacent to the R³ position and two atoms from
the point of attachment is optionally substituted with
R¹³, and a ring carbon or nitrogen adjacent to the R¹³
position and two atoms from the point of attachment is
optionally substituted with R¹³;

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R³³ is selected from the group consisting of hydrido, amidino, guanidino, carboxy, methoxy, ethoxy, isopropoxy, propoxy, hydroxy, amino, methoxyamino, ethoxyamino, acetamido, trifluoroacetamido, N-methylamino, dimethylamino, N-ethylamino, methylthio, ethylthio,

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isopropylthio, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3-pentafluoropropyl, trifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, chloro, bromo, amidosulfonyl, N-methylamidosulfonyl, N-methylamidosulfonyl, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 2,2,2-trifluoro-1-hydroxyethyl, methoxycarbonyl, ethoxycarbonyl, amidocarbonyl, n-methylamidocarbonyl, N-dimethylamidocarbonyl, cyano, and Q^b;

'n

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R¹⁶, R¹⁷, R¹⁸, and R¹⁹ are independently selected from the group consisting of hydrido, methyl, ethyl, isopropyl, carboxy, amidino, guanidino, methoxy, ethoxy, isopropoxy, propoxy, hydroxy, amino, dimethyl, 1-aminoethyl, 2-aminoethyl, N-methylamino, dimethylamino, N-ethylamino, methylthio, ethylthio, isopropylthio, trifluoromethylthio, methylsulfinyl, ethylsulfinyl, methylsulfinyl, ethylsulfinyl, pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,2-trifluoroethyl, 2,2,3-trifluoroethyl, 1,2,2,2 tetrafluoroethyl, bloom, hydroxymethyl, 1-hydroxymethyl, and consistent of the consisten

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tetrafluoroethoxy, fluoro, chloro, bromo, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, and cyano; R¹⁶ or R¹⁹ is optionally C(NR²⁹)NR²¹R²⁴ with the proviso

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that R¹⁶, R¹⁹, and Q² are not simultaneously hydrido; Q² is C(NR²⁹)NR²⁹R²⁴ or hydrido, with the proviso that no more than one of R²³ and R²⁴ is hydroxy at the same R23, R24, and R25 are independently selected from the group consisting of hydrido, methyl, ethyl, and hydroxy.

time;

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The more preferred specific embodiment compounds of Formula I having the formula:

or a pharmaceutically acceptable salt thereof, have common structural units, wherein;

M 18 N or N-O;

Ja is N or C-X0;

Jb is N or C-R1;

R' and X° are independently selected from the group consisting of hydrido, hydroxy, amino, amidino,

hydroxyamino, aminomethyl, 1-aminoethyl, methylamino, dimethylamino, cyano, methyl, ethyl, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, methoxy, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl,

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methoxyamino, methylthio, ethylthio, trifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, chloro, and bromo; R2 is Z0-Q;

Z° is selected from the group consisting of a bond, CH2, CH2CH2, O, S, NH, N(CH3), OCH2, SCH2, N(H)CH2, and N (CH₃) CH₂;

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adjacent to the carbon at the point of attachment of said carbon adjacent to R' and two atoms from the carbon at the phenyl or heteroaryl ring to Z° is optionally substituted pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, 4-pyridazinyl, and 1,3,5-triazin-2-yl, wherein a carbon point of attachment is optionally substituted by \mathbb{R}^{13} , a Q is selected from the group consisting of phenyl, 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3pyrazoly1, 2-thiazoly1, 3-jsoxazoly1, 5-isoxazoly1, 2pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-pyrazolyl, 4by R', the other carbon adjacent to the carbon at the pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-

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carbon adjacent to R13 and two atoms from the carbon at the point of attachment is optionally substituted by R12, and point of attachment is optionally substituted by R^{10} , a any carbon adjacent to both R10 and R12 is optionally substituted by R11;

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group consisting of hydrido, amidino, guanidino, carboxy, isopropoxy, propoxy, hydroxy, amino, N-methylamino, N,Nisopropylthio, trifluoromethyl, pentafluoroethyl, 2,2,2- $R^9,\ R^{11},\ and\ R^{13}$ are independently selected from the hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 2,2,2chloro, bromo, methanesulfonamido, amidosulfonyl, Ntrifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, methylamidocarbonyl, N,N-dimethylamidocarbonyl, and dimethylamino, N-ethylamino, methylthio, ethylthio, methyl, ethyl, propyl, isopropyl, methoxy, ethoxy, methylamidosulfonyl, N,N-dimethylamidosulfonyl, trifluoroethyl, 2,2,3,3,3-pentafluoropropyl, trifluoro-1-hydroxyethyl, amidocarbonyl, Ncyano;

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 R^{10} and R^{12} are independently selected from the group carboxymethyl, methyl, ethyl, propyl, isopropyl, methoxy consisting of hydrido, amidino, guanidino, carboxy ethoxy, isopropoxy, propoxy, hydroxy, amino, methoxyamino, ethoxyamino, acetamido,

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N,N-dimethylamidosulfonyl, hydroxymethyl, 1-hydroxyethyl, methanesulfonamido, amidosulfonyl, N-methylamidosulfonyl, benzylamidocarbonyl, N-(2-chlorobenzyl)amidocarbonyl, Naminoethyl, N-methylamino, dimethylamino, N-ethylamino, methoxycarbonyl, ethoxycarbonyl, amidocarbonyl, Nmethylamidocarbonyl, N,N-dimethylamidocarbonyl, Ntrifluoroacetamido, aminomethyl, 1-aminoethyl, 2-2-hydroxyethyl, 2,2,2-trifluoro-1-hydroxyethyl, (3-fluorobenzyl)amidocarbonyl, N-(2-

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phenylethyl)amidocarbonyl, N-benzylamidosulfonyl, N-(2trifluoromethylbenzyl) amidocarbonyl, N-(1phenylethyl) amidocarbonyl, N-(1-methyl-1-

difluorophenoxy, ,5-dimethylphenoxy, 3,4-dimethylphenoxy, cyclobutylamidocarbonyl, N-cyclopentylamidocarbonyl, Nbenzyloxy, 4-bromo-3-fluorophenoxy, 3-bromobenzyloxy, 4trifluoromethycyclohexylmethoxy, cyclopentoxy, benzyl, cyclohexylamidocarbonyl, fluoro, chloro, bromo, cyano, ylmethylamino, 4-butoxyphenamino, 3-chlorobenzyl, 4bromobenzyloxy, 4-bromobenzylamino, 5-bromopyrid-2isobutylamidocarbonyl, N-(2-butyl)amidocarbonyl, Ndifluorobenzyloxy, 4-difluoromethoxybenzyloxy, 2,3ethoxyphenoxy, 4-ethylbenzyloxy, 3-ethylphenoxy, 4chlorophenoxy, 4-chloro-3-ethylphenoxy, 4-chloro-3isopropylamidocarbonyl, N-propylamidocarbonyl, Nethylbenzylamino, 4-chloro-3-ethylphenylamino, 3-3,4-dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 4cyclobutoxy, cyclohexoxy, cyclohexylmethoxy, 4cyanopyrid-3-yloxy, 2,3-difluorobenzyloxy, 2,4chlorophenylsulfonyl, 5-chloropyrid-3-yloxy, 2difluorobenzyloxy, 3,4-difluorobenzyloxy, 2,5chlorobenzylsulfonyl, 4-chlorophenylamino, 4difluorobenzyloxy, 3,5-difluorophenoxy, 3,5difluorophenoxy, 2,4-difluorophenoxy, 2,5chlorobenzyloxy, 4-chlorobenzyloxy, 4-9 15 20

chlorobenzyl)amidosulfonyl, N-ethylamidocarbonyl, N-120

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Y° is selected from the group of formulas consisting 3-trifluoromethoxyphenoxy, 4-trifluoromethoxyphenoxy, 3trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3trifluoromethylthiobenzyloxy, 2,3,4-trifluorophenoxy, trifluoromethylbenzyloxy, 4-trifluoromethylbenzyloxy, 2,3,5-trifluorophenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy) phenoxy, and 3-2,4-bis-trifluoromethylbenzyloxy, 3trifluoromethylthiobenzyloxy, 4trifluoromethylthiophenoxy; 10

1-Qb-4-Qs-2-Rts-3-Rt7-5-Rts-6-Rt9benzene

fluorobenzyloxy, 2-fluoro-3-trifluoromethylbenzyloxy, 3-

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fluoro-5-trifluoromethylbenzyloxy, 4-fluoro-2-

ethylaminophenoxy, 3-ethyl-5-methylphenoxy, 4-

fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-

trifluoromethylbenzyloxy, 2-fluorophenoxy, 4-

trifluoromethylbenzyloxy, 4-fluoro-3-

fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-

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trifluoromethylphenoxy, 4-isopropylbenzyloxy, 3-

2-0b-5-0"-6-R17-4-R18-3-R19pyridine,

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nethylphenoxy, 4-isopropylbenzyloxy, 3-isopropylphenoxy,

4-isopropylphenoxy, 4-isopropyl-3-methylphenoxy,

phenylamino, 1-phenylethoxy, 2-phenylethoxy, 2-

35

phenylethyl, 2-phenylethylamino, phenylsulfonyl, 3-

lsopropylphenoxy, 4-isopropylphenoxy, 4-isopropyl-3-

3-Qb-6-Q-2-Rt6-5-Rt8-4-Rt9pyridine,

2-Qb-5-Q"-3-R16-6-R18pyrazine,

3-Qb-6-Q"-2-R19-5-R18-4-R19pyridazine,

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2-Q⁵-5-Q³-4-R¹⁷-6-R¹⁸pyrimidine,

5-Qb-2-Q4-4-R16-6-R19pyrimidine,

3-Q^b-5-Q*-4-R¹⁶-2-R¹⁹thiophene,

2-Q⁵-5-Q*-3-R¹⁶-4-R¹⁷thiophene,

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4-Q^-2-Q"-5-R19imidazole,

3-Q^b-5-Q"-4-R¹⁶-2-R¹⁹furan,

2-Qb-5-Qe-3-R16-4-R17furan,

 $2-Q^b-4-Q^a-5-R^{17}$ imidazole,

3-Qb-5-Q-4-R16isoxazole,

5-Qb-3-Q"-4-R16180xazole,

2-Q^b-5-Q^e-3-R¹⁶-4-R¹⁷pyrrole,

 $3-Q^{b}-5-Q^{a}-4-R^{16}-2-R^{19}pyrrole,$

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2-Q^b-5-Q°-4-R¹⁶pyrazole,

4-Qb-2-Q-5-Ribthiazole, and

2-Qb-5-Q*-4-R17thiazole;

 Q^{\bullet} is selected from the group consisting of a bond, CH, and CH,CH,.

In a most preferred specific embodiment of Formula I, compounds have the formula:

or a pharmaceutically acceptable salt thereof, wherein;

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B is selected from the group consisting of phenyl, 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrzolyl, 3-pyrzolyl, 2-imidazolyl, 3-isoxazolyl, 3-pyrazolyl, 4-imidazolyl, 3-isoxazolyl, and 5-isoxazolyl, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to A is optionally substituted by R³, the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R³, a carbon adjacent to R³ and two atoms from the carbon at the point of attachment is optionally substituted by R³, a carbon adjacent to R³ and two atoms from the carbon at the point of attachment is optionally substituted by R³, and any carbon adjacent to both R³ and R³ is optionally substituted by R³,

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R³³, R³⁴, R³⁵, and R³⁶ are independently selected from the group consisting of hydrido, amidino, guanidino, methyl, ethyl, methoxy, ethoxy, hydroxy, amino, N-methylamino, dimethylamino, methylthio, ethylthio, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, fluoro, chloro, bromo, amidosulfonyl, N-methylamidosulfonyl, hydroxymethyl, amidocarbonyl, carboxy, cyano, and Q^b;

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A is selected from the group consisting of a bond, NH, N(CH,), CH, CH, and CH, CH,;

Qb is NR²⁰R²¹ or C(NR²⁵)NR²³R²⁴;

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R¹⁰, R¹¹, R¹⁴, and R¹⁵ are independently selected from the group consisting of hydrido, methyl, and ethyl. In another most preferred specific embodiment of

In another most preferred specific embodiment of Formula I, compounds have the formula:

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or a pharmaceutically acceptable salt thereof, wherein;

2-butenyl, 2-butynyl, sec-butyl, tert-butyl, isobutyl, 2--methyl-2-butenyl, 3-methylbutyl, 3-methyl-2-butenyl, 1-3-heptynyl, 4-heptynyl, 5-heptynyl, 2-heptyl, 1-methyl-2neptenyl, 3-heptenyl, 4-heptenyl, 5-heptenyl, 2-heptynyl, nethyl-2-hexynyl, 1-methyl-3-hexynyl, 1-methyl-4-hexynyl, wherein each member of group B is optionally substituted pentynyl, 3-pentynyl, 2-pentyl, 3-pentyl, 2-methylbutyl, t any carbon up to and including 5 atoms from the point ethyl, 2-propenyl, 2-propynyl, propyl, isopropyl, butyl, B is selected from the group consisting of hydrido, 5,5,6,6,6-pentafluorohexyl, and 3,3,3-trifluoropropyl, rrifluoroethyl, 2,2-difluoropropyl, 4-trifluoromethylof attachment of B to A with one or more of the group hexyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 2-hexynyl, 3hexynyl, 4-hexynyl, 2-hexyl, 1-methyl-2-pentenyl, 1-3-heptyl, 1-ethyl-2-pentenyl, 1-ethyl-3-pentenyl, 1methylpropenyl, 1-pentyl, 2-pentenyl, 3-pentenyl, 2nexenyl, 1-methyl-3-hexenyl, 1-methyl-4-hexenyl, 1nethyl-3-pentenyl, 1-methyl-2-pentynyl, 1-methyl-3pentynyl, 3-hexyl, 1-ethyl-2-butenyl, 1-heptyl, 2- 5,5,5-trifluoropentyl, 4-trifluoromethylpentyl, ethyl-2-pentymyl, 1-ethyl-3-pentymyl, 2,2,2consisting of R12, R13, R14, R15, and R16,

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from the group consisting of hydrido, amidino, guanidino, R12, R13, R14, R15, and R16 are independently selected

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trifluoroethyl, fluoro, chloro, bromo, amidosulfonyl, Nmethylamino, dimethylamino, methoxyamino, methylthio, ethylthio, trifluoromethyl, pentafluoroethyl, 2,2,2methyl, ethyl, methoxy, ethoxy, hydroxy, amino, Nmethylamidosulfonyl, hydroxymethyl, amidocarbonyl, carboxy, cyano, and Qb;

A is selected from the group consisting of a bond, NH, N(CH3), CH2, CH3CH, and CH2CH2;

of CH,N(CH,), CH,N(CH,CH,), CH,CH,N(CH,), and CH,CH,N(CH,CH,) A is optionally selected from the group consisting with the proviso that B is hydrido;

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 \mathbb{Q}^{\flat} is selected from the group consisting of NR $^{^{10}}\mathrm{R}^{^{21}}$, R²⁰, R²¹, R²³, R²⁴, R²⁵, and R²⁶ are independently C(NR25) NR23R24, and N(R26) C(NR25) N(R21) (R24);

selected from the group consisting of hydrido, methyl, and ethyl.

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In still another most preferred specific embodiment of Formula I, compounds have the formula:

oxetan-3-yl, azetidin-1-yl, azetidin-2-yl, azetidin-3-yl, or a pharmaceutically acceptable salt thereof, wherein; cycloheptyl, oxalan-2-yl, 2-(2R)-bicyclo[2.2.1]-heptyl, bicyclo[3.1.0]hexan-6-yl, 2-morpholinyl, 3-morpholinyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, B is selected from the group consisting of

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piperidinyl, 2-piperidinyl, 3-piperidinyl, 4-piperidinyl, 1-pyrrolidinyl, 2-pyrrolidinyl, 3-pyrrolidinyl, 2-4-morpholinyl, 1-piperazinyl, 2-piperazinyl, 1-

dioxanyl, 2-tetrahydrofuranyl, 3-tetrahydrofuranyl, 2-tetrahydropyranyl, 4-tetrahydropyranyl, 4-tetrahydropyranyl, 4-tetrahydropyranyl, 2-tetrahydrothienyl, and 3-tetrahydrothienyl, wherein each ring carbon is optionally substituted with R³, ring carbons and a nitrogen adjacent to the carbon atom at the point of attachment are optionally substituted with R³ or R³, a ring carbon or nitrogen adjacent to the R³ position and two atoms from the point of attachment are optionally substituted with R³, and a ring carbon or nitrogen atom adjacent to the R³ position and two atoms from the point of attachment is optionally substituted with R³²,

R^{JJ} is selected from the group consisting of hydrido, amidino, guanidino, methyl, ethyl, methoxy, ethoxy, hydroxy, carboxy, amino, N-methylamino, dimethylamino, methoxyamino, methylthio, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, fluoro, chloro, bromo, amidosulfonyl, N-methylamidosulfonyl, hydroxymethyl, amidocarbonyl, cyano, and Q^b;

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A is selected from the group consisting of a bond, NH, N(CH,), CH, CH,CH, CH,CH, and CH,CH,CH,; Q^b is NR²⁰R²¹ or C(NR²³)NR²³R²⁴; R²⁰, R²¹, R²⁴, and R²⁵ are independently selected from the group consisting of hydrido, methyl, and ethyl. The most preferred specific embodiment compounds of Formula I said compounds having the formula:

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or a pharmaceutically acceptable salt thereof, have common structural units, wherein;

X° is selected from the group consisting of hydrido, hydroxy, amino, amidino, aminomethyl, cyano, methyl, trifluoromethyl, hydroxymethyl, chloro, and fluoro; R¹ is selected from the group consisting of hydrido, hydroxy, hydroxymethyl, amino, aminomethyl, methylamino, cyano, methyl, trifluoromethyl, methoxy, methylthio, trifluoromethoxy, fluoro, and chloro;

9

 R^2 is selected from the group consisting of phenyl, 2-thienyl, 2-furyl, 2-pyrrolyl, 2-imidazolyl, 2-thiazolyl, 3-isoxazolyl, 2-pyridyl, and 3-pyridyl, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to the pyridine ring is optionally substituted by R^2 , the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R^{13} , a carbon adjacent to R^{13} and two atoms from the carbon at the point of attachment is optionally substituted by R^{19} , a carbon adjacent to R^{13} and two atoms from the carbon at the point of attachment is optionally substituted by R^{12} , and any carbon adjacent to both R^{19} and R^{12} is optionally substituted by R^{12} , and any carbon adjacent to both R^{19}

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R, R1, and R1 are independently selected from the group consisting of hydrido, methyl, ethyl, methoxy, ethoxy, hydroxy, amino, N-methylamino, N,N-dimethylamino, methylthio, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, fluoro, chloro, bromo, amidosulfonyl, N-methylamidosulfonyl, NN-dimethylamidosulfonyl, hydroxymethyl, 1-hydroxyethyl, amidocarbonyl, N-methylamidocarbonyl, carboxy, and cyano,

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R¹⁰ and R¹² are independently selected from the group consisting of hydrido, amidino, amidocarbonyl, N-methylamidocarbonyl, N-benzylamidocarbonyl, N-(2-chlorobenzyl) amidocarbonyl, N-(3-

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fluorobenzyl) amidocarbonyl, N-(2trifluoromethylbenzyl) amidocarbonyl, N-(1-

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phenylethyl) amidocarbonyl, N-(1-methyl-1-phenylethyl) amidocarbonyl, N-benzylamidosulfonyl, N-(2-chlorobenzyl) amidocarbonyl, N-benzylamidocarbonyl, N-isopropylamidocarbonyl, N-isoputylamidocarbonyl, N-cyclobutylamidocarbonyl, N-cyclobutylamidocarbonyl, N-cyclopentylamidocarbonyl, N-cyclobetylamidocarbonyl, N-cyclopentylamidocarbonyl, N-cyclopentylamidocarbonyl, N-cyclopentylamidocarbonyl, N-cyclopentylamidocarbonyl, N-cyclopentylamidocarbonyl, N-cyclopentylamidocarbonyl, N-cyclopentylamidocarbonyl, amino, actamido, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, trifluoroacetamido, aminomethyl, N-methylamino, dimethylamino, methoxyamino, amidosulfonyl, N-methylamidosulfonyl, N-dimethylamidosulfonyl, methanesulfonamido, methoxycarbonyl, fluoro, chloro, bromo, and cyano;

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 Υ^{o} is selected from the group of formulas consisting .

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1-Qb-4-Q-2-R16-3-R17-5-R18-6-R19benzene,

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2-Qb-5-Q*-6-R17-4-R18-3-R18pyridine,

3-Qb-6-Q-2-R16-5-R18-4-R19pyridine,

3-Qb-5-Q*-4-R16-2-R19thiophene,

2-Q^b-5-Q^e-3-R¹⁶-4-R¹⁷thiophene,

3-Qb-5-Q"-4-R16-2-R19furan,

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2-Q^-5-Q"-3-R16-4-R17furan,

3-Q^b-5-Q*-4-R¹⁶-2-R¹⁹pyrrole,

2-Q^b-5-Q*-3-R¹⁶-4-R¹⁷pyrrole,

4-Qb-2-Q"-5-R19thiazole, and

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2-Qb-5-Q-4-R17thiazole;

R16, R17, R18, and R19 are independently selected from pentafluoroethyl, 2,2,2-trifluoroethyl, trifluoromethoxy, the group consisting of hydrido, methyl, ethyl, amidino, aminoethyl, 2-aminoethyl, N-methylamino, dimethylamino, guanidino, methoxy, hydroxy, amino, aminomethyl, 1fluoro, chloro, hydroxymethyl, carboxy, and cyano; methylsulfinyl, methylsulfonyl, trifluoromethyl, methylthio, ethylthio, trifluoromethylthio,

Q* is CH2.

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thrombus formation, and inhibiting embolus formation in a anticoagulant therapy for the treatment and prevention of preventing unstable angina, refractory angina, myocardial associated with the coagulation cascade and factors II, organs. The compounds also can be used for treating or mammal, in blood, in blood products, and in mammalian a variety of thrombotic conditions including coronary this invention can be used to inhibit serine protease artery and cerebrovascular disease. The compounds of invention can inhibit the formation of blood platelet VII, VIII, IX, X, XI, or XII. The compounds of the aggregates, inhibit the formation of fibrin, inhibit The compounds of this invention can be used in infarction, transient ischemic attacks, atrial 15 20

ocular build up of fibrin, and reocclusion or restenosis vein thrombosis, disseminated intravascular coagulation, also be used in prophylactic treatment of subjects who of recanalized vessels in a mammal. The compounds can fibrillation, thrombotic stroke, embolic stroke, deep

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prevention of cerebral vascular accident (CVA) or stroke. The compounds can be used to lower the risk of atherosclerosis. The compounds of Formula (I) would also be useful in are at risk of developing such disorders.

including mammals, rodents, and the like. More preferred compounds are also useful for veterinary treatment of Besides being useful for human treatment, these companion animals, exotic animals and farm animals, animals include horses, dogs, and cats.

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In yet another embodiment of the present invention, the novel compounds are selected from the compounds set forth in Examples 1 through 14.

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The use of generic terms in the description of the compounds are herein defined for clarity.

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construe the meaning of compounds based upon Formula A. Therefore, generally known in the art, should not be utilized to The generic terms described below are applicable these generic terms, unless otherwise indicated or solely for compounds based upon Formula I.

Standard single letter elemental symbols are used to atom. The symbol "H" represents a hydrido atom. Double represents a nitrogen atom. The symbol "P" represents a The symbol "N" elements of the periodical table (i.e., Cl represents phosphorus atom. The symbol "S" represents a sulfur letter elemental symbols are used as defined for the represent specific types of atoms unless otherwise The symbol "C" represents a carbon atom. chlorine, Se represents selenium, etc.). symbol "O" represents an oxygen atom.

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As utilized herein, the term "alkyl", either alone from 1 to about 10, preferably from 3 to about 8 carbon "alkylthio", means an acyclic alkyl radical containing Said alkyl radicals may be optionally substituted with atoms and more preferably 3 to about 6 carbon atoms. groups as defined below. Examples of such radicals or within other terms such as "haloalkyl" and

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isobutyl, sec-butyl, tert-butyl, pentyl, aminopentyl, include methyl, ethyl, chloroethyl, hydroxyethyl, npropyl, oxopropyl, isopropyl, n-butyl, cyanobutyl, iso-amyl, hexyl, octyl and the like.

The term "alkenyl" refers to an unsaturated, acyclic about 2 to about 10 carbon atoms, preferably from about 3 chloropropenyl, buten-1-yl, isobutenyl, penten-1-yl, 2-2to about 8 carbon atoms and more preferably 3 to about 6 hydroxyhexen-1-yl, hepten-1-yl, and octen-1-yl, and the hydrocarbon radical in so much as it contains at least Examples of one double bond. Such alkenyl radicals contain from carbon atoms. Said alkenyl radicals may be optionally methylbuten-1-yl, 3-methylbuten-1-yl, hexen-1-yl, 3suitable alkenyl radicals include propenyl, 2substituted with groups as defined below.

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10 carbon atoms, preferably having from about 3 to about The term "alkynyl" refers to an unsaturated, acyclic hydrocarbon radical in so much as it contains one or more triple bonds, such radicals containing about 2 to about hexyn-1-yl, hexyn-2-yl, hexyn-3-yl, 3,3-dimethylbutyn-1-8 carbon atoms and more preferably having 3 to about 6 Examples of pentyn-2-yl, 4-methoxypentyn-2-yl, 3-methylbutyn-1-yl, carbon atoms. Said alkynyl radicals may be optionally hydroxypropynyl, butyn-1-yl, butyn-2-yl, pentyn-1-yl, suitable alkynyl radicals include ethynyl, propynyl, substituted with groups as defined below. yl radicals and the like.

hydrido radical may be attached to a carbon atom to form a "methine" radical -CH=, or two hydrido radicals may be attached to a carbon atom to form a "methylene" (-CH2-) (H). This hydrido radical may be attached, for example, The term "hydrido" denotes a single hydrogen atom to an oxygen atom to form a "hydroxyl" radical, one radical.

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The term "carbon" radical denotes a carbon atom without any covalent bonds and capable of forming four covalent bonds.

The term "cyano" radical denotes a carbon radical having three of four covalent bonds shared by a nitrogen

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The term "hydroxyalkyl" embraces radicals wherein any one or more of the alkyl carbon atoms is substituted with a hydroxyl as defined above. Specifically embraced are monohydroxyalkyl, dihydroxyalkyl and polyhydroxyalkyl radicals.

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The term "alkanoyl" embraces radicals wherein one or more of the terminal alkyl carbon atoms are substituted with one or more carbonyl radicals as defined below. Specifically embraced are monocarbonylalkyl and dicarbonylalkyl radicals. Examples of monocarbonylalkyl radicals include formyl, acetyl, and pentanoyl. Examples of dicarbonylalkyl radicals include oxalyl, malonyl, and succinyl.

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The term "alkylene" radical denotes linear or branched radicals having from 1 to about 10 carbon atoms and having attachment points for two or more covalent bonds. Examples of such radicals are methylene, ethylene, and isopropylidene.

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The term "alkenylene" radical denotes linear or branched radicals having from 2 to about 10 carbon atoms, at least one double bond, and having attachment points for two or more covalent bonds. Examples of such radicals are 1,1-vinylidene (CH₂-C), 1,2-vinylidene (-CH=CH-), and 1,4-butadienyl (-CH=CH-CH=CH-).

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The term "halo" means halogens such as fluorine, chlorine, bromine or iodine atoms.

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The term "haloalkyl" embraces radicals wherein any one or more of the alkyl carbon atoms is substituted with halo as defined above. Specifically embraced are monohaloalkyl, dihaloalkyl and polyhaloalkyl radicals. A

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monohaloalkyl radical, for one example, may have either a bromo, chloro or a fluoro atom within the radical. Dihalo radicals may have two or more of the same halo atoms or a combination of different halo radicals and polyhaloalkyl radicals may have more than two of the same halo atoms or a combination of different halo radicals. More preferred haloalkyl radicals are "haloalkyl" radicals having one to about six carbon atoms. Examples of such haloalkyl radicals include fluoromethyl, difluoromethyl,

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trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, trifluoroethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl and dichloropropyl.

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The term "hydroxyhaloalkyl" embraces radicals wherein any one or more of the haloalkyl carbon atoms is substituted with hydroxy as defined above. Examples of "hydroxyhaloalkyl" radicals include hexafluorohydroxypropyl.

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The term "haloalkylene radical" denotes alkylene radicals wherein any one or more of the alkylene carbon atoms is substituted with halo as defined above. Dihalo alkylene radicals may have two or more of the same halo atoms or a combination of different halo radicals and polyhaloalkylene radicals may have more than two of the same halo atoms or a combination of different halo radicals. More preferred haloalkylene radicals are "haloalkylene" radicals having one to about six carbon atoms. Examples of "haloalkylene" radicals include difluoromethylene, tetrafluoroethylene, alkyl substituted monofluoromethylene, and aryl substituted

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The term "haloalkenyl" denotes linear or branched radicals having from 1 to about 10 carbon atoms and having one or more double bonds wherein any one or more

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:rifluoromethylene.

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of the alkenyl carbon atoms is substituted with halo as defined above. Dihaloalkenyl radicals may have two or more of the same halo atoms or a combination of different halo radicals and polyhaloalkenyl radicals may have more than two of the same halo atoms or a combination of different halo radicals.

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luoropropoxy. Examples of such haloalkoxyalkyl radicals The terms "alkoxy" and "alkoxyalkyl" embrace linear include methoxy, ethoxy, propoxy, butoxy, isopropoxy and tert-butoxy alkyls. The "alkoxy" radicals may be further "haloalkoxyalkyl" radicals. Examples of such haloalkoxy substituted with one or more halo atoms, such as fluoro, Iluoroethoxy, tetrafluoroethoxy, pentafluoroethoxy, and preferred alkoxy radicals are "alkoxy" radicals having methoxy radical. The term "alkoxyalkyl" also embraces or branched oxy-containing radicals each having alkyl crifluoromethoxy, difluoromethoxy, trifluoroethoxy, one to six carbon atoms. Examples of such radicals portions of one to about ten carbon atoms, such as rifluoromethoxymethyl, difluoromethoxyethyl, and alkyl radicals having one or more alkoxy radicals monoalkoxyalkyl and dialkoxyalkyl radicals. More include fluoromethoxymethyl, chloromethoxyethyl, attached to the alkyl radical, that is, to form adicals include fluoromethoxy, chloromethoxy, chloro or bromo, to provide "haloalkoxy" and crifluoroethoxymethyl.

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The terms "alkenyloxy" and "alkenyloxyalkyl" embrace linear or branched oxy-containing radicals each having alkenyl portions of two to about ten carbon atoms, such as ethenyloxy or propenyloxy radical. The term "alkenyloxyalkyl" also embraces alkenyl radicals having one or more alkenyloxy radicals attached to the alkyl radical, that is, to form monoalkenyloxyalkyl and dialkenyloxyalkyl radicals. More preferred alkenyloxy radicals are "alkenyloxy" radicals having two to six

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carbon atoms. Examples of such radicals include ethenyloxy, propenyloxy, butenyloxy, and isopropenyloxy alkyls. The "alkenyloxy" radicals may be further substituted with one or more halo atoms, such as fluoro, chloro or bromo, to provide "haloalkenyloxy" radicals. Examples of such radicals include trifluoroethenyloxy, fluoroethenyloxy, difluoroethenyhoxy, and fluoropropenyloxy.

The term "haloalkoxyalkyl" also embraces alkyl radicals having one or more haloalkoxy radicals attached to the alkyl radical, that is, to form monohaloalkoxyalkyl and dihaloalkoxyalkyl radicals. The term "haloalkenyloxy" also embraces oxygen radicals having one or more haloalkenyloxy radicals attached to the oxygen radical, that is, to form monohaloalkenyloxy and dihaloalkenyloxy radicals. The term "haloalkenyloxyalkyl" also embraces alkyl radicals having one or more haloalkenyloxy radicals attached to the alkyl radical, that is, to form monohaloalkenyloxyalkyl and

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The term "alkylenedioxy" radicals denotes alkylene radicals having at least two oxygens bonded to a single alkylene group. Examples of "alkylenedioxy" radicals include methylenedioxy, ethylenedioxy, alkyleubstituted methylenedioxy, and arylsubstituted methylenedioxy. The term "haloalkylenedioxy" radicals denotes haloalkylene radicals having at least two oxy groups bonded to a single haloalkyl group. Examples of "haloalkylenedioxy, radicals include difluoromethylenedioxy,

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dihaloalkenyloxyalkyl radicals.

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radicals include difluoromethylenedioxy, tetrachloroethylenedioxy, tetrachloroethylenedioxy, alkylsubstituted monofluoromethylenedioxy, and arylsubstituted monofluoromethylenedioxy.

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The term "aryl", alone or in combination, means a carbocyclic aromatic system containing one, two or three rings wherein such rings may be attached together in a pendant manner or may be fused. The term "fused" means

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that a second ring is present (ie, attached or formed) by having two adjacent atoms in common (ie, shared) with the 'condensed". The term "aryl" embraces aromatic radicals such as phenyl, naphthyl, tetrahydronaphthyl, indane and first ring. The term "fused" is equivalent to the term biphenyl.

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such as phenyl, naphthyl, tetrahydronaphthyl, indane and biphenyl wherein the aryl radical is substituted with 3 The term "perhaloaryl" embraces aromatic radicals or more halo radicals as defined below.

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of saturated heterocyclic radicals include saturated 3 to piperidino, piperazinyl, etc.]; saturated 3 to 6-membered carbon, nitrogen, sulfur and oxygen, wherein at least one contain one, two or three rings wherein such rings may be neteromonocyclic group containing 1 to 2 oxygen atoms and l to 3 nitrogen atoms (e.g. morpholinyl, etc.); saturated to 6-membered heteromonocyclic group containing 1 to 2 pyrrolinyl, 3-pyrrolinyl, pyrrolindinyl, 1,3-dioxolanyl, attached in a pendant manner or may be fused. Examples defined herein. Preferred heterocyclic radicals include radicals having from 4 through 15 ring members, herein partially saturated heteroatom-containing ring-shaped ring atom is a heteroatom. Heterocyclyl radicals may thiazolidinyl, etc.]. Examples of partially saturated like. Said "heterocyclyl" group may be substituted as limiting examples of heterocyclic radicals include 2dihydropyran, dihydrofuran and dihydrothiazole. Nonmorpholinyl, 1,4-dithianyl, thiomorpholinyl, and the The term "heterocyclyl" embraces saturated and referred to as "C4-C15 heterocycly1", selected from 5-membered heteromonocylic group containing 1 to 4 2H-pyranyl, 4H-pyranyl, piperidinyl, 1,4-dioxanyl, nitrogen atoms[e.g. pyrrolidiny], imidazolidiny], heterocyclyl radicals include dihydrothiophene, sulfur atoms and 1 to 3 nitrogen atoms [e.g.,

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heteromonocyclic group containing 1 to 2 oxygen atoms and etc.]; unsaturated 5 to 6-membered heteromonocyclic group carbon, nitrogen, sulfur and oxygen, wherein at least one contain one, two or three rings wherein such rings may be 1 to 3 nitrogen atoms, for example, oxazolyl, isoxazolyl, heterocyclic group containing 1 to 5 nitrogen atoms, for oxadiazolyl [e.g., 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, to 3 nitrogen atoms [e.g. benzoxazoly1, benzoxadiazoly1, [e.g., 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3heterocyclic group containing 1 to 2 oxygen atoms and 1 containing 1 to 4 nitrogen atoms, for example, pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl The term "heteroaryl" embraces fully unsaturated benzotriazolyl, tetrazolopyridazinyl [e.g., tetrazolo triazolyl, etc.] tetrazolyl [e.g. 1H-tetrazolyl, 2Hmembered heteromonocyclic group containing an oxygen containing a sulfur atom, for example, 2-thienyl, 3-1,2,5-oxadiazoly1, etc.] etc.; unsaturated condensed [1,5-b]pyridazinyl, etc.], etc.; unsaturated 3 to 6heteroatom-containing ring-shaped aromatic radicals ring atom is a heteroatom. Heteroaryl radicals may atom, for example, pyranyl, 2-furyl, 3-furyl, etc.; having from 4 through 15 ring members selected from heteromonocyclyl group of 5 to 6 contiguous members unsaturated 5 to 6-membered heteromonocyclic group of "heteroaryl" radicals, include the unsaturated benzimidazolyl, quinolyl, isoquinolyl, indazolyl, attached in a pendant manner or may be fused. tetrazolyl, etc.], etc.; unsaturated condensed thienyl, etc.; unsaturated 5- to 6-membered example, indolyl, isoindolyl, indolizinyl, 20 30 10 15 25

containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms,

thiadiazoly1, 1,3,4-thiadiazoly1, 1,2,5-thiadiazoly1,

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live to twelve membered fused or unfused radicals.

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for example, thiazoly1, thiadiazoly1 [e.g., 1,2,4-

etc.] etc.; unsaturated condensed heterocyclic group

containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., benzothiazolyl, benzothiadiazolyl, etc.] and the 11ke. The term also embraces radicals where heterocyclic radicals are fused with aryl radicals. Examples of such fused blcyclic radicals include benzofuran,

benzothlophene, and the like. Said "heteroaryl" group may be substituted as defined herein. Preferred heteroaryl radicals include five and six membered unfused radicals. Non-limiting examples of heteroaryl radicals include 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3-thienyl, 4-pyrrolyl, 4-imidazolyl, 1,2,4-triazol-3-yl, 1,2,4-triazol-5-yl, 1,3,4-oxadiazol-3-yl, 1,2,4-triazol-5-yl, 1,3,4-oxadiazol-3-yl, 1,2,4-triazol-5-yl, 1,3,4-oxadiazol-3-yl, 3-isothiazolyl, 2-oxazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 2-pyridyl, 4-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-pyrimidinyl, 4-pyridazinyl, 5-pyrazinyl, 4-pyridazinyl, 1,2,4-triazin-3-yl, 1,2,4-triazin-3-yl, 1,2,4-triazin-3-yl, 1,2,4-triazin-3-yl, and 1,2,3-triazin-5-yl, and the like.

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The term "sulfonyl", whether used alone or linked to other terms such as alkylsulfonyl, denotes respectively divalent radicals -SO₂-. "Alkylsulfonyl", embraces alkyl radicals attached to a sulfonyl radical, where alkyl is defined as above. "Alkylsulfonylalkyl", embraces alkylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above. "Haloalkylsulfonyl", embraces haloalkyl radicals attached to a sulfonyl radical, where haloalkyl is defined as above. "Haloalkylsulfonylalkyl", embraces haloalkylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above.

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The term "amidosulfonyl" embraces amino, monoalkylamino, dialkylamino, monocycloalkylamino, alkyl cycloalkylamino, dicycloalkylamino, N-alkyl-N-arylamino, arylamino, aralkylamino, nitrogen containing

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heterocyclyl, heterocyclylamino, N-alkyl-N-heterocyclylamino, heteroarylamino, and heteroaralkylamino radicals, attached to one of two unshared bonds in a sulfonyl radical.

The term "sulfinyl", whether used alone or linked to other terms such as alkylsulfinyl, denotes respectively divalent radicals -S(O) - "Alkylsulfinyl", embraces alkyl radicals attached to a sulfinyl radical, where alkyl is defined as above. "Alkylsulfinylalkyl", embraces alkylsulfinyl radicals attached to an alkyl radical, where alkyl is defined as above. "Haloalkylsulfinyl radical, attached to a sulfinyl radical, where haloalkyl is defined as above. "Haloalkylsulfinyl radicals attached to an alkyl radical, where alkyl is defined as above.

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The term "aralkyl" embraces aryl-substituted alkyl radicals. Preferable aralkyl radicals are "aralkyl" radicals having aryl radicals attached to alkyl radicals having one to six carbon atoms. Examples of such radicals include benzyl, diphenylmethyl, triphenylmethyl, phenylmethyl and diphenylethyl. The terms benzyl and phenylmethyl are interchangeable.

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The term "heteroaralkyl" embraces heteroarylsubstituted alkyl radicals wherein the heteroaralkyl radical may be additionally substituted with three or more substituents as defined above for aralkyl radicals. The term "perhaloaralkyl" embraces aryl-substituted alkyl radicals wherein the aralkyl radical is substituted with three or more halo radicals as defined above.

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The term "aralkylsulfinyl", embraces aralkyl radicals attached to a sulfinyl radical, where aralkyl is defined as above. "Aralkylsulfinylalkyl", embraces aralkylsulfinyl radicals attached to an alkyl radical,

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where alkyl is defined as above.

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The term "aralkylsulfonyl", embraces aralkyl radicals attached to a sulfonyl radical, where aralkyl is defined as above. "Aralkylsulfonylalkyl", embraces aralkylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above.

adicals having three to ten carbon atoms and one or more The term "cycloalkyl" embraces radicals having three to 15 carbon atoms. More preferred cycloalkyl radicals cycloalkylalkyl" embraces cycloalkyl-substituted alkyl seven carbon atoms. Examples include radicals such as are "cycloalkyl" radicals having three to seven carbon atoms. Examples include radicals such as cyclopropyl, cycloalkylalkyl" radicals having cycloalkyl radicals erm cycloalkyl embraces radicals having seven to 15 cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl. radicals are "cycloalkenyl" radicals having three to carbon atoms and having two to four rings. Exmaples carbon-carbon double bonds. Preferred cycloalkenyl attached to alkyl radicals having one to six carbon Preferable cycloalkylalkyl radicals are syclohexylhexyl. The term "cycloalkenyl" embraces oicyclo[2.2.1]heptyl) and adamantyl. The term cyclobutenyl, cyclopentenyl, cyclohexenyl and atoms. Examples of such radicals include Incude radicals such as norbornyl (i.e.,

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cycloheptenyl. The term "halocycloalkyl" embraces radicals wherein any one or more of the cycloalkyl carbon atoms is substituted with halo as defined above. Specifically embraced are monohalocycloalkyl, dihalocycloalkyl and polyhalocycloalkyl radicals. A monohalocycloalkyl radical, for one example, may have either a bromo, chloro or a fluoro atom within the radical. Dihalo radicals may have two or more of the same halo atoms or a combination of different halo radicals and polyhalocycloalkyl radicals may have more than two of the same halo atoms or a combination of different halo

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radicals. More preferred halocycloalkyl radicals are "halocycloalkyl" radicals having three to about eight carbon atoms. Examples of such halocycloalkyl radicals include fluorocyclopropyl, difluorocyclobutyl, trifluorocyclopentyl, tetrafluorocyclohexyl, and dichlorocyclopentyl. The term "halocycloalkenyl" embraces radicals wherein any one or more of the cycloalkenyl carbon atoms is substituted with halo as defined above. Specifically embraced are monohalocycloalkenyl, dihalocycloalkenyl and

polyhalocycloalkenyl radicals.

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The term "cycloalkoxy" embraces cycloalkyl radicals attached to an oxy radical. Examples of such radicals includes cyclohexoxy and cyclopentoxy. The term "cycloalkoxyalkyl" also embraces alkyl radicals having one or more cycloalkoxy radicals attached to the alkyl radical, that is, to form monocycloalkoxyalkyl and dicycloalkoxyalkyl radicals. Examples of such radicals include cyclohexoxyethyl. The "cycloalkoxy" radicals may be further substituted with one or more halo atoms, such as fluoro, chloro or bromo, to provide "halocycloalkoxy" and "halocycloalkoxyalkyl" radicals.

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The term "cycloalkylalkoxy" embraces cycloalkyl radicals attached to an alkoxy radical. Examples of such radicals includes cyclohexylmethoxy and cyclopentylmethoxy.

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The term "cycloalkenyloxy" embraces cycloalkenyl radicals attached to an oxy radical. Examples of such radicals includes cyclohexenyloxy and cyclopentenyloxy. The term "cycloalkenyloxyalkyl" also embraces alkyl radicals having one or more cycloalkenyloxy radicals attached to the alkyl radical, that is, to form monocycloalkenyloxyalkyl and dicycloalkenyloxyalkyl radicals. Examples of such radicals include cyclohexenyloxyethyl. The "cycloalkenyloxy" radicals may be further substituted with one or more halo atoms, such

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as fluoro, chloro or bromo, to provide "halocycloalkenyloxyalkyl" radicals.

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The term "cycloalkylenedioxy" radicals denotes cycloalkylene radicals having at least two oxygens bonded to a single cycloalkylene group. Examples of "alkylenedioxy" radicals include 1,2-dioxycyclohexylene.

The term "cycloalkylsulfinyl", embraces cycloalkyl radicals attached to a sulfinyl radical, where cycloalkyl is defined as above. "Cycloalkylsulfinylalkyl", embraces cycloalkylsulfinyl radicals attached to an alkyl radical, where alkyl is defined as above. The term "Cycloalkylsulfonyl", embraces cycloalkyl radicals attached to a sulfonyl radical, where cycloalkyl is defined as above. "Cycloalkylsulfonyl radicals, embraces cycloalkylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above.

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The term "cycloalkylalkanoyl" embraces radicals wherein one or more of the cycloalkyl carbon atoms are substituted with one or more carbonyl radicals as defined below. Specifically embraced are monocarbonylcycloalkyl and dicarbonylcycloalkyl radicals. Examples of monocarbonylcycloalkyl radicals include cyclohexylcarbonyl, cyclohexylacetyl, and cyclopentylcarbonyl. Examples of dicarbonylcycloalkyl radicals include 1,2-dicarbonylcyclohexane.

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The term "alkylthio" embraces radicals containing a linear or branched alkyl radical, of one to ten carbon atoms, attached to a divalent sulfur atom. More preferred alkylthio radicals are "alkylthio" radicals having one to six carbon atoms. An example of "alkylthio" is methylthio (CH.S-). The "alkylthio" radicals may be further substituted with one or more halo atoms, such as fluoro, chloro or bromo, to provide "haloalkylthio" radicals. Examples of such radicals include fluoromethylthio, chloromethylthio, trifluoromethylthio,

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difluoromethylthio, trifluoroethylthio, fluoroethylthio, tetrafluoroethylthio, pentafluoroethylthio, and

fluoropropylthio.

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The term "alkyl aryl amino" embraces radicals containing a linear or branched alkyl radical, of one to ten carbon atoms, and one aryl radical both attached to an amino radical. Examples include N-methyl-4-methoxyaniline, N-ethyl-4-methoxyaniline, and N-methyl-4-trifluoromethoxyaniline.

The term alkylamino denotes "monoalkylamino" and "dialkylamino" containing one or two alkyl radicals, respectively, attached to an amino radical. One or two alkyl radicals of the alkylamino may be optionally substituted with hydrogen bonding substitutents selected from the group consisting of hydroxy, amino, monoalkylamino, dialkylamino, amidino, quanidino, thiol, and alkoxy provided the alkyl radicals comprises two or more carbons.

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The terms arylamino denotes "monoarylamino" and "diarylamino" containing one or two aryl radicals, respectively, attached to an amino radical. Examples of such radicals include N-phenylamino and N-naphthylamino.

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The term "aralkylamino", embraces aralkyl radicals attached to an amino radical, where aralkyl is defined as above. The term aralkylamino denotes "monoaralkylamino" and "diaralkylamino" containing one or two aralkyl radicals, respectively, attached to an amino radical. The term aralkylamino further denotes "monoaralkyl monoalkylamino" containing one aralkyl radical and one alkyl radical attached to an amino radical.

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The term "arylaulfinyl" embraces radicals containing an aryl radical, as defined above, attached to a divalent S(O) atom. The term "arylaulfinylalkyl" denotes arylsulfinyl radicals attached to a linear or branched alkyl radical, of one to ten carbon atoms.

The term "arylsulfonyl", embraces aryl radicals attached to a sulfonyl radical, where aryl is defined as above. "arylsulfonylalkyl", embraces arylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above. The term "heteroarylsulfinyl" embraces radicals containing an heteroaryl radical, as defined above, attached to a divalent S(0) atom. The term "heteroarylsulfinylalkyl" denotes heteroarylsulfinyl radical, of one to ten carbon atoms. The term "Heteroarylsulfonyl", embraces heteroaryl radicals attached to a sulfonyl radical, where heteroaryl is defined as above. "Heteroarylsulfonylalkyl", embraces heteroarylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above.

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The term "aryloxy" embraces aryl radicals, as defined above, attached to an oxygen atom. Examples of such radicals include phenoxy, 4-chloro-3-ethylphenoxy, 4-chloro-3-methylphenoxy, 3-chloro-4-ethylphenoxy, 3,4-dichlorophenoxy, 4-methylphenoxy, 3-trifluoromethylphenoxy, 4-fluorophenoxy, 3,4-dimethylphenoxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 4-fluoro-3-methylphenoxy, 5,6,7,8-tetrahydronaphthyloxy, 3-isopropylphenoxy, 3-cyclopropylphenoxy, 3-ctrahydronaphthyloxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy)

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phenoxy, and 4-tert -butylphenoxy.

The term "aroyl" embraces aryl radicals, as defined above, attached to an carbonyl radical as defined above.

Examples of such radicals include benzoyl and toluoyl.

The term "aralkanoyl" embraces aralkyl radicals, as defined herein, attached to an carbonyl radical as defined above. Examples of such radicals include, for example, phenylacetyl.

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The term "aralkoxy" embraces oxy-containing aralkyl radicals attached through an oxygen atom to other

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radicals. More preferred aralkoxy radicals are "aralkoxy" radicals having phenyl radicals attached to alkoxy radical as described above. Examples of such radicals include benzyloxy, 1-phenylethoxy, 3-trifluoromethoxybenzyloxy, 3-trifluoromethylbenzyloxy, 3,5-difluorobenyloxy, 2-fluoro-3-trifluoromethylbenzyloxy, and

2-phenylethoxy.
The term "aryloxyalkyl" embraces aryloxy radicals,

as defined above, attached to an alkyl group.

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Examples

of such radicals include phenoxymethyl.

The term "haloaryloxyalkyl" embraces aryloxyalkyl
radicals, as defined above, wherein one to five halo
radicals are attached to an aryloxy group.

The term "heteroaroyl" embraces heteroaryl radicals, as defined above, attached to an carbonyl radical as defined above. Examples of such radicals include furoyl and nicotinyl.

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The term "heteroaralkanoyl" embraces heteroaralkyl radicals, as defined herein, attached to an carbonyl radical as defined above. Examples of such radicals include, for example, pyridylacetyl and furylbutyryl.

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The term "heteroaralkoxy" embraces oxy-containing heteroaralkyl radicals attached through an oxygen atom to other radicals. More preferred heteroaralkoxy radicals are "heteroaralkoxy" radicals having heteroaryl radicals attached to alkoxy radical as described above. The term "heterocyclylalkoxy" embraces oxy-containing heterocyclylalkyl radicals attached through an oxygen atom to other radicals.

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The term "haloheteroaryloxyalkyl" embraces heteroaryloxyalkyl radicals, as defined above, wherein one to four halo radicals are attached to an heteroaryloxy group.

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The term "heteroarylamino" embraces heteroaryl radicals, as defined above, attached to an amino group.

Examples of such radicals include pyridylamino. The term "heterocyclylamino" embraces heterocyclyl radicals, as 152

Examples of such radicals include pyridylmethylamino. The The term "heteroaralkylamino" embraces heteroaralkyl term "heterocyclylalkylamino" embraces heterocyclylalkyl radicals, as defined above, attached to an amino group. radicals, as defined above, attached to an amino group.

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defined above, attached to an amino group.

heterocyclyl radicals, as defined above, attached to an radicals, as defined above, attached to an oxy group. Examples of such radicals include 2-thiophenyloxy, 2-The term "heteroaryloxy" embraces heteroaryl pyrimidyloxy, 2-pyridyloxy, 3-pyridyloxy, and 4pyridyloxy. The term "heterocyclyloxy" embraces oxy group.

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The term "heteroaryloxyalkyl" embraces heteroaryloxy "heterocyclyloxyalkyl" embraces heterocyclyloxy radicals, Examples of such radicals include 2-pyridyloxymethyl, 3radicals, as defined above, attached to an alkyl group. pyridyloxyethyl, and 4-pyridyloxymethyl. The term as defined above, attached to an alkyl group.

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defined above, attached to an sulfur atom. Examples of The term "arylthio" embraces aryl radicals, as such radicals include phenylthio.

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The term "arylthioalkyl" embraces arylthio radicals, as defined above, attached to an alkyl group. Examples Examples of such radicals include methylthiomethyl. The term "alkoxyalkyl" embraces alkoxy radicals, as defined radicals, as defined above, attached to an alkyl group. above, attached to an alkyl group. Examples of such The term "alkylthioalkyl" embraces alkylthio of such radicals include phenylthiomethyl.

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atom. The term "carboxy" embraces a hydroxyl radical, as The term "carbonyl" denotes a carbon radical having two of the four covalent bonds shared with an oxygen radicals include methoxymethyl.

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defined above, attached to one of two unshared bonds in a one carboalkoxy radical, as defined above, attached to an above, attached to an alkyl group. The term "carboalkoxy" carbonyl group. The term "monocarboalkoxyalkyl" embraces embraces alkoxy radicals, as defined above, attached to one of two unshared bonds in a carbonyl group. The term alkyl group. The term "dicarboalkoxyalkyl" embraces two arylamino, arylamino, aralkylamino, nitrogen containing radicals, as defined above, attached to an alkyl group. "carboaralkoxy" embraces aralkoxy radicals, as defined carboalkoxy radicals, as defined above, attached to an alkylene group. The term "monocyanoalkyl" embraces one carbonyl group. The term "carboxamido" embraces amino, "carboxyalkyl" embraces a carboxy radical, as defined cyano radical, as defined above, attached to an alkyl "carboxamidoalkyl" embraces carboxamido radicals, as defined above, attached to an alkyl group. The term group. The term "dicyanoalkylene" embraces two cyano The term "carboalkoxycyanoalkyl" embraces one cyano heteroaralkylamino radicals, attached to one of two alkylcycloalkylamino, dicycloalkylamino, N-alkyl-Nmonoalkylamino, dialkylamino, monocycloalkylamino, above, attached to one of two unshared bonds in a unshared bonds in a carbonyl group. The term heterocyclyl, heterocyclylamino, N-alkyl-Nradical, as defined above, attached to an heterocyclylamino, heteroarylamino, and carboalkoxyalkyl group. Ŋ 10 15 20 25

alkylsulfonylalkyl, aralkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, alkylthio, arylthio, amino, alkylamino, dialkylamino, aralkoxy, arylthio, and alkylthioalkyl. carbonyl or thionocarbonyl group bonded to a radical alkynyl, haloalkyl, alkoxy, alkoxyalkyl, haloalkoxy, selected from, for example, hydrido, alkyl, alkenyl, aryl, heterocyclyl, heteroaryl, alkylsulfinylalkyl,

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The term "acyl", alone or in combination, means a

Examples of "acyl" are formyl, acetyl, benzoyl, trifluoroacetyl, phthaloyl, malonyl, nicotinyl, and the like. The term "haloalkanoyl" embraces one or more halo radicals, as defined herein, attached to an alkanoyl radical as defined above. Examples of such radicals include, for example, chloroacetyl, trifluoroacetyl, bromopropanoyl, and heptafluorobutanoyl.

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The term "phosphono" embraces a pentavalent phosphorus attached with two covalent bonds to an oxygen radical. The term "dialkoxyphosphono" denotes two alkoxy radicals, as defined above, attached to a phosphono radical with two covalent bonds. The term "diaralkoxyphosphono" denotes two aralkoxy radicals, as defined above, attached to a phosphono radicals, as defined above, attached to an alkyl radicals, as defined above, attached to an alkyl radical. The term "diaralkoxyphosphonoalkyl" denotes diaralkoxyphosphono radicals, as defined above, attached to an alkyl radical.

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radical having two of the four covalent bond sites shared alkyl and having two covalent bonds available for bonding C=NH, C=NCH, C=NOH, and unsubstituted amino group bonded to one of two available to a single atom such as carbon. Examples of such imino The term "amino" denotes a nitrogen atom containing radicals include, for example, -NH2, -NHCH3, -NHOH, and two substituents such as hydrido, hydroxy or alkyl and containing one substituent such as hydrido, hydroxy or The term "amidino" embraces a substituted or =NH, =NCH3, =NOH, and with an imino group. Examples of such imino carbonyl having one covalent bond available for bonding to a bonds of an iminocarbonyl radical. Examples of such The term "imino carbonyl" denotes a carbon single atom such as carbon. Examples of such amino NHOCH;. The term "imino" denotes a nitrogen atom radicals include, for example, radicals include, for example,

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amidino radicals include, for example, NH₃-C=NH, NH₃-C=NCH₃, NH₃-C=NCH₃, NH₃-C=NOCH₃ and CH₃NH-C=NOH. The term "guanidino" denotes an amidino group bonded to an amino group as defined above where said amino group can be bonded to a third group. Examples of such guanidino radicals include, for example, NH₃-C(NH)-NH-, NH₃-C(NCH₃)-NH-, and CH₃NH-C(NOH)-NH-.

The term "sulfonium" denotes a positively charged trivalent sulfur atom where said sulfur is substituted with three carbon based groups such as alkyl, alkenyl, aralkyl, or aryl. The term "dialkyl sulfonium" denotes a sulfonium group where said sulfur is substituted with two alkyl groups. Examples of such dialkylsulfonium radicals include, for example, (CH₃)₃S⁻. The term "dialkyl sulfonium alkyl denotes a dialkyl sulfonium group where said group is bonded to one bond of an alkylene group as defined above. Examples of such dialkylsulfoniumalkyl radicals include (CH₃)₃S⁻-CH₄CH₅.

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The term "phosphonium" denotes a positively charged tetravalent phosphorus atom where said phosphorus is substituted with four carbon based groups such as alkyl, alkenyl, aralkyl, or aryl. The term "trialkyl phosphonium" denotes a phosphonium group where said phosphorus is substituted with three alkyl groups. Examples of such trialkylphosphonium radicals include, for example, (CH,),P+-.

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said "alkyl", "alkenyl", "alkynyl", "alkanoyl",
"alkylene", "alkenylene", "hydroxyalkyl", "haloalkyl",
"haloalkylene", "haloalkenyl", "alkoxy", "alkenyloxy",
"alkenyloxyalkyl", "alkoxyalkyl", "aryl", "perhaloaryl",
"haloalkoxy", "haloalkoxyalkyl", "haloalkenyloxy",
"haloalkoxylkyl", "alkylenedioxy",
"haloalkylenedioxy", "heterocyclyl", "heteroaryl",
"hydroxyhaloalkyl", "alkylsulfonyl", "haloalkylsulfonyl",
"alkylsulfinylalkyl", "haloalkylsulfonylalkyl",
"alkylsulfinyl", "alkylsulfinylalkyl",

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halocycloalkenyloxyalkyl", "alkylthio", "haloalkylthio", arylsulfinylalkyl", "arylsulfonyl", "arylsulfonylalkyl", heteroarylamino", "heteroaralkylamino", "heteroaryloxy", 'cycloalkylalkanoyl", "cycloalkylalkyl", "cycloalkenyl", heteroaryloxylalkyl", "aryloxy", "aroyl", "aralkanoyl", optionally have 1 or more non-hydrido substituents such cycloalkoxy", "cycloalkoxyalkyl", "cycloalkylalkoxy", alkylsulfinyl", "amino", "oxy", "thio", "alkylamino", perhaloaralkyl, aralkylgulfonyl, aralkylgulfonylalkyl, ıralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, haloalkylsulfinylalkyl", "aralkyl", "heteroaralkyl", heteroaroyl", "heteroaralkanoyl", "heteroaralkoxy", heteroaralkoxyalkyl", "arylthio", "arylthioalkyl", neteroaryloxy, heteroaryloxylalkyl, haloalkylthio, dialkylsulfoniumalkyl" groups defined above may heteroarylamino-N-alkylamino, heteroaralkylamino, heteroarylsulfinyl", "heteroarylsulfinylalkyl", 'heteroarylsulfonyl", "heteroarylsulfonylalkyl", cycloalkylsulfinyl", "cycloalkylsulfinylalkyl", cycloalkylsulfonyl", "cycloalkylsulfonylalkyl" aralkoxy", "aryloxyalkyl", "haloaryloxyalkyl", 'alkoxyalkyl", "acyl", "amidino", "guanidino", 'dialkylsulfonium", "trialkylphosphonium", and 'halocycloalkoxyalkyl", "halocycloalkenyloxy", 'arylamino", "aralkylamino", "arylsulfinyl", cycloalkylsulfonylalkyl, heteroarylamino, Ncycloalkylsulfinylalkyl, cycloalkylsulfonyl, trialkylphosphonium, dialkylsulfoniumalkyl, cycloalkenyloxy", "cycloalkenyloxyalkyl", aralkylsulfonylalkyl", "aralkylsulfinyl", as amidino, guanidino, dialkylsulfonium, cycloalkylenedioxy", "halocycloalkoxy" halocycloalkyl", "halocycloalkenyl", nalocycloalkenyl, cycloalkylsulfinyl, aralkylsulfinylalkyl", "cycloalkyl" perhaloaralkyl", "aralkylsulfonyl"

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carboxyalkyl, carboalkoxy, alkoxycarbonyl, carboaralkoxy, cycloalkenyl, cycloalkylalkyl, cycloalkenylalkyl, halo, cycloalkoxyalkyl, cycloalkylalkoxy, cycloalkenyloxyalkyl aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, halocycloalkenyloxyalkyl, hydroxy, amino, thio, nitro, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, aralkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, phosphono, phosphonoalkyl, diaralkoxyphosphono, and alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, haloalkylenedioxy, cycloalkyl, cycloalkylalkanoyl, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, heteroarylsulfinyl, heteroarylsulfonyl, alkanoyl, alkylamino, alkylthio, alkylthioalkyl, arylamino, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, heteroaralkyl, arylalkenyl, heteroarylalkenyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, arylalkyl, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, arylsulfinyl, arylsulfonyl, heteroarylthio, alkenyloxy, alkenyloxyalky, alkylenedioxy, alkenoyl, aroyl, heteroaroyl, aralkanoyl, halocycloalkoxyalkyl, halocycloalkenyloxy, hydroxyaralkyl, hydroxyalkyl, aminoalkyl, monoarylamidosulfonyl, arylsulfonamido, aralkylamino, arylthio, arylthioalkyl, arylsulfinylalkyl, arylsulfonylalkyl, cycloalkylenedioxy, halocycloalkoxy, alkylsulfonyl, alkylsulfonylalkyl, diaralkoxyphosphonoalkyl. 10 12 35 20 25 30

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CH(OR24)-, =C(OR24)-, S(O)2CH2-, and -NR24CH2- and many other stoms with a side chain. The chain may be constituted of neteroarylalkyl, heteroaryloxyalkyl, heteroarylthioalkyl, The term "spacer" can include a covalent bond and a OCF20-, -0(CF2)20-, -S-, -S(0)-, -S(0)2-, -N(H)-, -N(H)0-, $-N(R^{2a})O_-$, $-N(R^{2a})_-$, $-C(O)_-$, $-C(O)_ -C(O)_ -C(O)_-$ -N=, $-C(O)_-$ -N=, $-C(O)_ -C(O)_ -C(O)_-$ -C(Oradicals defined above or generally known or ascertained one or more radicals selected from: alkylene, alkenyl, selected from alkyl, alkenyl, alkynyl, aryl, heteroaryl, atoms or a straight chain of 1 or 2 or 3 or 4 or 5 or 6 constituted by a radical selected from =C(H) -, $=C(R^{24})$ -, substituents such as 1 or more non-hydrido substituents and heteroarylalkenyl. Multi-valent chains may consist The spacer may have 1 to 7 atoms of a univalent O-, -S-, -S(O)-, -S(O)2-, -NH-, -N(R20)-, -N=, -CH(OH)-, =C(OH)-, -CH(OR2*)-, =C(OR2*)-, and -C(O)- wherein \mathbb{R}^{2a} is .O-, -O-CH₂-, -S-CH₃-, -CH₃CH₂-, ethenyl, -CH=CH(OH)-, -OCH2-, -SCH2-, S(0) CH2-, -CH2C(0)-, -CH(OH)-, =C(OH)-, of a straight chain of 1 or 2 or 3 or 4 or 5 or 6 or 7 arylthioalkyl, cycloalkyl, cycloalkylalkyl, haloalkyl, OCH30-, -0 (CH3) 20-, -NHCH3-, -OCH (R24) 0-, -0 (CH2CHR24) 0-, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, linear moiety having a backbone of 1 to 7 contiguous by one of skill-in-the art, Side chains may include sralkyl, aryloxyalkyl, alkoxyalkyl, alkylthioalkyl, alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, heteroaryloxy, heteroaryloxylalkyl, haloalkylthio, heteroarylamino-N-alkylamino, heteroaralkylamino, or multi-valent chain. Univalent chains may be such as amidino, guanidino, dialkylsulfonium, naloalkenyl, haloalkoxyalkyl, perhaloaralkyl, cycloalkylsulfonylalkyl, heteroarylamino, Ncycloalkylaulfinylalkyl, cycloalkylaulfonyl, trialkylphosphonium, dialkylsulfoniumalkyl, halocycloalkenyl, cycloalkylsulfinyl,

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cycloalkoxyalkyl, cycloalkylalkoxy, cycloalkenyloxyalkyl heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, carboxyalkyl, carboalkoxy, carboaralkoxy, carboxamido, halocycloalkenyloxyalkyl, hydroxy, amino, thio, nitro, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, cycloalkylalkyl, cycloalkenylalkyl, halo, haloalkyl, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, aralkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, heteroarylsulfinyl, heteroarylsulfonyl, alkanoyl, alkylamino, alkylthio, alkylthioalkyl, arylamino, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, heteroarylalkyl, arylalkenyl, heteroarylalkenyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, heteroaryloxy, heteroaryloxyalkyl, arylalkyl, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, partially saturated heterocyclyl, heteroaryl, haloalkylenedioxy, cycloalkyl, cycloalkenyl, alkenyloxy, alkenyloxyalky, alkylenedioxy, arylsulfinyl, arylsulfonyl, heteroarylthio. haloalkenyl, haloalkoxy, hydroxyhaloalkyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, halocycloalkoxyalkyl, halocycloalkenyloxy, hydroxyaralkyl, hydroxyalkyl, aminoalkyl, phosphonoalkyl, diaralkoxyphosphono, and monoarylamidosulfonyl, arylsulfonamido, aralkylamino, arylthio, arylthioalkyl, arylsulfinylalkyl, arylsulfonylalkyl cycloalkylenedioxy, halocycloalkoxy alkyløulfonyl, alkyløulfonylalkyl, diaralkoxyphosphonoalkyl. 20 25 30 ហ 10 15

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Formula A Embodiment

invention is directed to compounds falling within Formula A. In general, the compounds of formula I are a subset the symbols employed to depict the chemical groups for In addition to those compounds falling within the scope of Formula I, in another embodiment, the present depict the chemical groups for Formula A correspond to embodiment of the invention, the symbols employed to of compounds falling within Formula I. In this Formula I as follows:

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Formula A

wherein

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X, corresponds to the ring atom adjacent to M and Ja; X, corresponds to M;

X, corresponds to the ring atom that is the point of attachment for K;

X, corresponds to the ring atom that is the point of attachment for R2;

X, corresponds to Jb;

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X, corresponds to Ja;

 L_1 corresponds to -A- Ψ -;

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Z₁ corresponds to B;

 L_3 corresponds to -K-E⁰-;

 Z_{a} corresponds to Y^{0} ;

L, and Z, corresponds to R2.

In one embodiment of the present invention, the compounds correspond to Formula A:

$$\begin{bmatrix} x_6 & x_5 & x_4 & x_4 & x_4 & x_5 \\ x_1 & x_2 & x_3 & x_4 & x_5 & x_5 \\ x_2 & x_3 & x_4 & x_5 & x_5 \\ x_3 & x_4 & x_5 & x_5 & x_5 \\ x_4 & x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 & x_5 \\ x_5 & x_5 & x_5 & x_5 & x_5 \\ x_$$

wherein:

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X1, X2, X1 X4, X5, and X4 are each ring atoms defining a 6 membered heterocyclic or aromatic ring; X_1 , X_2 , and X_4 are independently carbon or nitrogen; X, is carbon;

or sulfur, provided at least one of $X_1,\ X_4$, and X_6 is other X, and X, are independently carbon, nitrogen, oxygen than carbon when X, is carbon;

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covalently bonded to $X_{\rm i}$, $Z_{\rm j}$ is covalently bonded to $X_{\rm i}$, and 24, respectively, are covalently bonded to different ring independently being a covalent bond or comprising one or $L_1,\ L_3$ and L_4 are linkages through which $Z_1,\ Z_3,$ and atoms of the 6 membered heterocyclic or aromatic ring more atoms through which $Z_1,\ Z_3,\ and\ Z_4$ are covalently Z, is covalently bonded to X,, each of L,, L, and L, defined by X_1 , X_2 , X_3 , X_4 , X_5 , and X_6 , wherein Z_1 is bonded to X_1 , X_3 and X_4 , respectively,

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amidine, guanidine, amino, or aminoalkyl group, the ring membered substituted heterocyclic or aromatic ring, the substituents of the hydrocarbyl or ring comprising an atoms of the 5 or 6 membered heterocyclic or aromatic ring of Z, being carbon, sulfur, nitrogen, or oxygen, Z, is a substituted hydrocarbyl, or a 5 or 6

wherein the 5 or 6 membered ring is optionally substituted at any position with halogen, hydroxy, or alkyl;

Z_t comprises hydrocarbyl, substituted hydrocarbyl or a 5 or 6-membered heterocyclic ring, the ring atoms of the 5 or 6-membered heterocyclic ring being carbon, sulfur, nitrogen or oxygen;

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 $\mathbf{Z_{1}} \text{ is hydrogen, hydrocarbyl, or substituted} \\ \text{hydrocarbyl; and} \\$

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2, is a hydrogen bond acceptor covalently or datively bonded to X₂.
In yet another embodiment the compounds correspond

to Formula A wherein: X_1, X_2, X_3, X_4, X_5 , and X_6 are each ring atoms defining

6 membered heterocyclic or aromatic ring;

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 $X_{\mathtt{l}}$, $X_{\mathtt{l}}$, and $X_{\mathtt{l}}$ are independently carbon or nitrogen,

X, is carbon;

 X_{5} and X_{6} are independently carbon, nitrogen, oxygen or sulfur, provided at least one of X_{1} , X_{4} , and X_{6} is other than carbon when X_{5} is carbon,

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L₁, L₂ and L₄ are linkages through which Z₁, Z₂, and Z₄, respectively, are covalently bonded to different ring atoms of the 6 membered heterocyclic or aromatic ring defined by X₁, X₂, X₃, X₄, X₅, and X₆, wherein Z₁ is covalently bonded to X₁, Z₂ is covalently bonded to X₄, and L₄, independently being a covalent bond or comprising one or more atoms through which Z₁, Z₃, and Z₄ are covalently bonded to X₁, X₃ and X₄, respectively;

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Z, comprises a 5 or 6 membered heterocyclic or aromatic ring substituted with an amidine group, the ring atoms of the 5 or 6 membered heterocyclic or aromatic ring of Z, being carbon, sulfur, nitrogen, or oxygen, wherein the 5 or 6 membered ring is optionally substituted at any position with halogen, hydroxy, or alkyl;

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 Z_{4} comprises a 5 or 6 membered heterocyclic or carboxylic ring, the ring atoms of the 5 or 6 membered heterocyclic or carboxylic ring of Z_{4} being carbon, nitrogen, oxygen, or sulfur;

Z, is hydrocarbyl or substituted hydrocarbyl; and Z, is a hydrogen bond acceptor covalently or datively bonded to X,.

In one preferred embodiment, when X₂ is carbon Z₂ is hydrogen, fluorine, oxygen, or sulfur. A further embodiment provides compounds that when X₂ is nitrogen Z₃ is hydrogen, an electron pair, or a hydrogen bond acceptor. In yet another embodiment when X₂ is nitrogen Z₂, is hydrogen or oxygen. Exemplary 6 membered heterocyclic or aromatic rings defined by X₁, X₂, X₃, X₄, X₅, and X₆ include pyridone, pyrimidone, triazinone, azaquinone, pyrazinone, pyridine, pyrazine, pyrimidine,

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diagrammer, pyrazimene, reoxazimene, pyrimidine, dihydrotriazimedione, pyridine, pyrazime, pyrimidine, triazime. For each of these embodiments, X, may be optionally substituted with a halogen.

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Exemplary Z, substituents include substituted or unsubstituted C, to C, alkyl, substituted or unsubstituted C, to C, cycloalkyl and substituted or unsubstituted phenyl. Exemplary preferred Z, substituents include substituted or unsubstituted cyclopropyl, isobutyl, sec-butyl, methyl, ethyl, and phenyl.

Exemplary L₁ linkages include -X₅NH- wherein X₅ is covalently bonded directly to Z₁ and X₅ is a direct bond or -(CH₂)_m- wherein m is 1 to 5. An exemplary preferred L₁ linkage is -X₅NH- wherein X₅ is covalently bonded directly to Z₁ and X₂ is a direct bond or -(CH₂)_m- wherein m is 1 to 2. A particularly exemplary L₁ linkage is -X₅NH- wherein X₅ is covalently bonded directly to Z₁ and is a direct bond. In a further embodiment, L₁ may covalently bond to X₆ to form a fused ring.

An exemplary Z, group is a substituted, 6 member, carbocyclic aromatic ring. In an exemplary preferred embodiment, Z, has the following structure:

Wherein

Exemplary R,2 substituent is amino.

Exemplary R₄₄ substituents include hydrogen, hydrocarbyl, substituted hydrocarbyl, heterocyclo, halogen or a substituted or unsubstituted heteroatom selected from nitrogen, oxygen, sulfur and phosphorous. Exemplary preferred R₄₄ substituents include hydrogen, hydrocarbyl, substituted hydrocarbyl, heteroaryl, heterocyclo, halogen, acetamido, guanidino, hydroxy, nitro, amino, amidosulfonyl, acylamido, hydroxy, substituted hydrocarbyloxy, hydrocarbylthio, substituted hydrocarbylsulfonyl, or substituted hydrocarbylsulfonyl, particularly exemplary R₄₄ substituents include hydroxy, alkylsulfonyl, haloalkyl, carboxamidoalkyl, or carboxamidoalkylaryl.

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Exemplary R₄₁, R₄₃ and R₁₅ substituents include hydrogen, and hydrocarbyl, substituted hydrocarbyl, halogen or an optionally substituted hetero atom selected from the group consisting of oxygen, nitrogen, and sulfur. Particularly exemplary R₄₁, R₄₃ and R₄₅ substituents include hydrogen and halogen.

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An exemplary L_t linkage is -(CH₂)_n- where m is 0 to 5. A more exemplary L_t linkage is -(CH₂)_n- where m is 0 to 2. An even more exemplary L_t linkage is a direct bond.

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2, is substituted with a amidine group. In a particularly any embodiment set forth, Z, may be optionally substituted hydrolysis, oxidation, reduction or elimination yields an amidine group. In yet another preferred embodiment, the 5 or 6 membered heterocyclic or aromatic ring comprising In a particularly preferred embodiment, the 5 or 6 membered heterocyclic or aromatic ring comprising Z, is elimination yields an amidine group. Additionally, in either an amidine group or with a derivatized amidine at any position with a halogen, alkyl, hydroxy or any combination thereof. Exemplary substitutions include preferred embodiment, Z, is benzene substituted with substituted with a derivatized amidine which, upon fluorine, methyl, hydroxy, CF, or any combination which, upon hydrolysis, oxidation, reduction or thereof.

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Accordingly, in one embodiment Z, is -R₃₀₀C(=NR₃₀₁)NR₃₀₂R₃₀₃, wherein R₃₀₀ is a 6 membered carbocyclic aromatic ring, R₃₀₁, R₃₀₂, R₃₀₃ are independently selected from hydrogen, optionally substituted hyrocarbyl, and optionally substituted hetero atoms selected from the group consisting of oxygen, nitrogen, phosphorous and sulfur.

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In yet another embodiment Z, is a benzamidine derivative which hydrolyzes under physiological conditions to form benzamidine, the benzamidine derivative having the formula

S(=0),OR, S(=0),SR and alkene, provided that the carbon provided, however, at least one of R301, R302, and R303 is group consisting of hydrogen, C(=0)R, S(=0)OR, S(=0)SR atom directly bonded to the amidine is sp2 hybridized, R₃₀₁, R₃₀₂, and R₃₀₃ are independently selected from the other than hydrogen;

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R is hydrocarbyl, substituted hydrocarbyl, or heterocycle;

 R_{104} is halogen, hydrogen, hydroxyl, alkyl, sulfhydryl, alkoxy, and thioalkyl;

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R₃₀₅ is oxygen, sulfur, halogen, hydrogen, hydroxyl, alkyl, sulfhydryl, alkoxy, and thioalkyl;

R₁₀₆ is halogen, hydrogen, hydroxyl, alkyl,

sulfhydryl, alkoxy, and thioalkyl; and

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R30, is oxygen, sulfur, halogen, hydrogen, hydroxyl, alkyl, sulfhydryl, alkoxy, and thioalkyl.

derivative which oxidizes under physiological conditions In still a further embodiment, Z_3 is a benzamidine to form benzamidine, the benzamidine derivative having the formula

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hydrocarbyl and aryl, provided, however, (i) at least one of $R_{101},\ R_{102},\ and\ R_{103}$ is other than hydrogen and (1i) the group consisting of hydrogen, optionally substituted R₃₀₁, R₃₀₂, and R₃₀₃ are independently selected from the carbon atom directly bonded to the amidine is sp hybridized when R, 101, R, 102, and R, 101 is optionally substituted hydrocarbyl;

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R104 is halogen, hydrogen, hydroxyl, alkyl, sulfhydryl, alkoxy, and thioalkyl;

R₃₀₅ is oxygen, sulfur, halogen, hydrogen, hydroxyl,

alkyl, sulfhydryl, alkoxy, and thioalkyl;

R, is halogen, hydrogen, hydroxyl, alkyl,

S

R,,, is oxygen, sulfur, halogen, hydrogen, hydroxyl, alkyl, sulfhydryl, alkoxy, and thioalkyl. sulfhydryl, alkoxy, and thioalkyl; and

In a further embodiment, Z, is a benzamidine conditions to form benzamidine, the benzamidine derivative which is reduced under physiological derivative having the formula

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-NR, or -N(R)2, wherein each R is independently optionally $R_{\rm joi}$, $R_{\rm joi}$, and $R_{\rm joj}$ are independently hydrogen, -OR, -SR, substituted hydrocarbyl, or heterocylo, provided,

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however, at least one of R₃₀₁, R₃₀₂, and R₃₀₃ is other than hydrogen;

R₁₀₄ is halogen, hydrogen, hydroxyl, alkyl, sulfhydryl, alkoxy, and thioalkyl; R, is oxygen, sulfur, halogen, hydrogen, hydroxyl, alkyl, sulfhydryl, alkoxy, and thioalkyl;

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R, is halogen, hydrogen, hydroxyl, alkyl,

R,0, is oxygen, sulfur, halogen, hydrogen, hydroxyl, sulfhydryl, alkoxy, and thioalkyl; and

alkyl, sulfhydryl, alkoxy, and thioalkyl.

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derivative which undergoes an elimination reaction under In yet another embodiment, Z, is a benzamidine

physiological conditions to form benzamidine, the benzamidine derivative having the formula

R₁₀₁, R₁₀₂, and R₁₀₃ are independently (i) hydrogen, (11) substituted hydrocarbyl wherein the carbon bonded to the amidine group is substituted with -OCR₄, -SR₄, -NR₆, or -N(R₆), wherein each R₆ is independently -C(O)R₅, -C(O)NR₆, and each R₆ is independently hydrocarbyl, substituted hydrocarbyl or heterocyclo, (iii) substituted alkyl with the carbon atom beta to the point of attachment to the amidine group being an unsaturated electron withdrawing group, provided, at least one of R₁₀₁, R₁₀₂, and R₁₀₃ is other than hydrogen;

R₃₀₄ is halogen, hydrogen, hydroxyl, alkyl, sulfhydryl, alkoxy, and thloalkyl;

R₁₀₈ is oxygen, sulfur, halogen, hydrogen, hydroxyl, alkyl, sulfhydryl, alkoxy, and thioalkyl;
R₁₀₈ is halogen, hydrogen, hydroxyl, alkyl,

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2

 $R_{\rm jos}$ is halogen, hydrogen, hydroxyl, alkyl, sulfhydryl, alkoxy, and thioalkyl; and

R₁₀, is oxygen, sulfur, halogen, hydrogen, hydroxyl, alkyl, sulfhydryl, alkoxy, and thioalkyl.

Exemplary L₁ linkages include a glycine derivative, an alanine derivative, an amino derivative, and a sulfonyl derivative. A more exemplary L₁ linkage is a

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glycine derivative.

In one preferred embodiment, the compounds
corresponding to formula (A) are represented by the
following structure:

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Exemplary substituents of compounds having this structure for each of X_1 , X_2 , X_3 , X_4 , X_5 , and X_6 are as described for structural formula (A). Preferably, X_9 is a direct bond or -(CH₂)_B- where m is 1 or 2. Exemplary Z_1 , Z_2 , Z_3 , and Z_4 groups are also as described for structural formula (A).

In yet another embodiment, compounds represented by structural formula A may form fused rings with the following structure:

wherein

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Exemplary groups for $Z_1,\ Z_2,\ Z_4,\ L_3,\ X_1,\ X_2,\ X_3,\ X_4,$ and X_5 are as defined above,

X is independently carbon or nitrogen;

 X_{γ} and X_{φ} are independently a covalent bond, carbon, nitrogen, oxygen or sulfur;

R,0 is not present when X, is a bond and Rg0 is not present R, and R, are independently selected from the group either unsubstituted or substituted with hydroxy, amino, C1-C6 alkyl, C3-C8 cycloalkyl, or halogen provided that atoms to which each is attached, form a 5 or 6 membered substituted hydrocarbyl, aryl, wherein aryl is phenyl when X₈ is a bond; or R,0 and R₈₀, along with the ring consisting of hydrogen, halogen, amino, hydrocarbyl, n is 0 to 2; and saturated ring.

yields an amidine group, and Z, is selected from the group benzene substituted with two substituents, R,2 and R44, and and phenyl. In an exemplary preferred embodiment, Z, is consisting of cyclopropyl, isopropyl, methyl cyclobutyl, other of R, and R, is covalently bonded to the other of said beta positions. Preferred and exemplary R42 and R44 reduction or elimination under physiological conditions covalently bonded to one of said beta positions and the direct bond, Z, is a substituted, 6 member, carbocyclic derivatized amidine which, upon hydrolysis, oxidation, compounds corresponding to formula A, wherein X, is a wo ring atoms each of which is in the beta position covalently linked to X,, wherein one of R, and R,, is Among the preferred embodiments, therefore, are relative to the ring atom of Z, through which Z, is promatic ring, Z, is benzene substituted with a groups are as described above.

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z, is a substituted, 6 member, carbocyclic aromatic ring, $\mathbf{z_{3}}$ is benzene substituted with an amidine group and $\mathbf{z_{1}}$ is corresponding to formula A, wherein X, is a direct bond, In yet another preferred embodiment, are compounds selected from the group consisting of cyclopropyl, isopropyl, methyl cyclobutyl, and phenyl. In an

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Preferred and exemplary R₁₂ and R₁₄ groups are as described with two substituents, R,2 and R,4, and two ring atoms each exemplary preferred embodiment, Z, is benzene substituted wherein one of R42 and R44 is covalently bonded to one of atom of $Z_{\mbox{\tiny 4}}$ through which $Z_{\mbox{\tiny 4}}$ is covalently linked to $X_{\mbox{\tiny 4}}$, covalently bonded to the other of said beta positions. of which is in the beta position relative to the ring said beta positions and the other of R,2 and R,4 is above.

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oxidation, and elimation. For illustrative purposes, the corresponding to structural formula A, having one or more prodrug moiety is covalently bonded to the amidine group biological mechanisms. In general terms, these prodrug biologically active drug by a number of chemical and following paragraphs detail prodrugs in which the Any prodrug compound of the present invention prodrug moieties as part of the molecule, can be conversion mechanisms are hydrolysis, reduction, on Z, as depicted in structural formula A above. converted under physiological conditions to the

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Conversion of the prodrug to the biologically active enzymatically hydrolyzable with water. The reaction with group would be a carbonyl derivative an example of which carbon acid. Other suitable hydrolyzable derivatives of water must further result in the removal of the prodrug drug. An example of a prodrug derivative at the amidine amidine group of the drug by removal of the acyl as the carbonyl of the amide nitrogen) results in freeing the drug can be accomplished by hydrolysis of the prodrug moiety and the liberation of the biologically active is N-acyl. Hydrolysis (the addition of water to the moiety provided the prodrug moiety is chemically or the amidine include carbonyl, thiocarbonyl, imine, enamine, and oxgenated sulfur.

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Conversion of the prodrug to the biologically active drug can be additionally accomplished by reduction of the

prodrug moiety provided the prodrug moiety is reducible under physiological conditions in the presence of a reducing enzymatic process. The reduction must further result in the removal of the prodrug moiety and the liberation of the biologically active drug. An example of a reducible prodrug derivative at the amidine group would be an oxygen containing group in which an oxygen is directly attached to the amidine. Reduction (the addition of hydrogen to amidine ntrogen and the oxygen) results in freeing the amidine group of the drug by removal of the oxygen as water or an alcohol. Other suitable reducible prodrug derivatives of the amidine include a nitrogen containing group, and a sulfur are each in their most reduced state.

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iberation of the biologically active drug. An example of results in forming an oxygenated intermediate that breaks of the amidine include saturated hydrocarbyl, unsaturated Conversion of the prodrug to the biologically active prodrug moiety provided the prodrug moiety is oxidizable residue. Other suitable oxidizable prodrug derivatives oxidative enzymatic process. The oxidation must further under physiological conditions in the presence of an drug can be also be accomplished by oxidation of the oxidizable prodrug derivative at the amidine group carbon beta to the carbon directly connected to the result in the removal of the prodrug moiety and the would be hydrocarbyl containing unsaturation in the concurrent hydrolysis of the oxygenated hydrocarbyl umidine group. Oxidation (the addition of oxygen) down freeing the amidine group of the drug with substituted hydrocarbyl, aryl, and aralkyl.

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Conversion of the prodrug to the biologically active drug can further be accomplished by elimination of the prodrug moiety provided the prodrug moiety is removed under physiological conditions with a chemical or

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of the biologically active drug. An general example of an withdrawing group bonded to the carbon beta to the carbon would be a hydrocarbyl containing an unsaturated electron carbon directly bonded to the amidino group. Elimination more pieces) results in the freeing of the amidine group oxygen, nitrogen or sulfur at the carbon directly bonded biological reaction. The elimination must further result in the removal of the prodrug moiety and the liberation Other suitable eliminateable prodrug derivatives of the hydrocarbyl group could have a cyano group beta to the of the drug with concurrent removal of the unsaturated directly connected to the amidine. More specifically, (a reaction in which a molecule fragments into two or eliminateable prodrug derivative at the amidine group amidine include a hydrocarbyl substituted at the beta nitro, or sulfonyl or an alkyl group substituted with hydrocarbyl residue derived from the prodrug moiey. carbon with carbonyl, alkoxycarbonyl, amidocarbonyl, for illustration purposes and exemplification, the

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to the amidine group.

Any prodrug compound of the present invention corresponding to formula A may undergo any combination of the above detailed mechanisms to convert the prodrug to the biologically active compound. For example, a particular compound may undergo hydrolysis, oxidation, elimination, and reduction to convert the prodrug to the biologically active compound. Equally, a particular

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In a particular preferred embodiment, the compound represented by Formula A above is selected from the group of compounds illustrated in Table 1 below.

compound may undergo only one these mechanisms to convert

the prodrug to the biologically active compound.

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Compound NZ N Σ, Σ Compound No.

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Compound ZZ Z TABLE 1 Compound No.

Compound

Compound No.

H₂N

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Compound Į, Compound 80. 11

H₂N

Examples or elsewhere herein, the following specific compounds, as depicted in Table 2, having any one of the three structural formulas below may be prepared. Pollowing the processes described in the Schemes,

As employed herein, unless otherwise indicated, "core" refers to the 6-membered heterocyclic or aromatic

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ring to which Z₁, Z₃ and Z₄, through their respective linkages, are attached. For illustrative purposes, each core as defined by structural formula I, II, or III above and as listed in Table 2 below are specifically set forth. In addition, the cores below specifically depict the point of attachment of Z₁, Z₂ and Z₄ to said core.

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AZAQUINONE

PYRIMIDINE

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Again, for illustrative purposes, each R** group listed in Table 2 is set forth below

НО

 CF_3

hydroxy

carboxamidobenzyl

isobutyramido

isobutoxy

NH2

атіпо

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TABLE 2

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1sobutyleulfonyl trifluoromethyl ž hydroxy methyl
or
isopropyl
or
cyclopropyl
or
phenyl
methyl
or
ethyl
or
cyclobutyl
or
cyclobutyl
or
ethyl
or
cyclobutyl
or
ethyl
or
ethyl
or
cyclobutyl ethyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
phenyl methyl or Pyridone Pyridone Pyridone

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Core	$\mathbf{z_1}$	R ⁴⁴
Pyridone	methyl	carboxamidobenzyl
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Pyridone	methyl	carboxamidobuty1-2-
	or	yl
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	•
	phenyl	
Pyridone	methyl	isobutyramido
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	io	
	cyclobutyl	
	or	
	phenyl	

isobutoxy

methyl

Core

Pyridone

or cyclopropyl

or ethyl or isopropyl

or cyclobutyl or

phenyl

Pyridone

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1sobutyleulfonyl ¥. hydroxy amino cyclopropyl
or
cyclobutyl
or
phenyl
methyl
or
ethyl
or
cyclopropyl
or
cyclopropyl
or
cyclobutyl
or methyl
or
ethyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
phenyl methyl
or
ethyl
or
isopropyl Core Pyrimidone Pyrimidone Pyridone

carboethoxy

carboxyl

methyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
phenyl
methyl
or
isopropyl
or
cyclopropyl
or
cyclopropyl
or
isopropyl
or
or
cyclopropyl
or
or
or

Pyridone

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trifluoromethyl ¥.

methyl

Core

Pyrimidone

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1sobutyramido ž, carboethoxy isobutoxy ethyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
phenyl
methyl
or
ethyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl methyl
or
ethyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
phenyl methyl or phenyl Core Pyrimidone Pyrimidone Pyrimidone

carboxamidobenzyl

Pyrimidone

cyclopropyl

ethyl or isopropyl or

or cyclobutyl or

phenyl
methyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
phenyl

carboxamidobutyl-2-yl

or cyclopropyl

isopropyl

methyl or ethyl or

Pyrimidone

or cyclobutyl or phenyl

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carboxyl hydroxy amino methyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
isopropyl
or
isopropyl
or
cyclobutyl
or
ethyl
or
isopropyl
or
cyclobutyl
or
isopropyl
or
cyclobutyl
or
phenyl
or
cyclobutyl
or
phenyl
or
cyclobutyl
or
isopropyl
or
cyclobutyl Triazinone Pyrimidone Core Pyrimidone

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Core	$\mathbf{z_i}$	R ⁴⁴
Triazinone	methyl	isobutylsulfonyl
	or	
	ethyl	
	or	
	isopropyl	
	or	
,	cyclopropyl	
	or	
	cyclobutyl	
	or	,
	phenyl	
Triazinone	methyl	trifluoromethyl
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Triazinone	methyl	carboxamidobenzy1
	or	
	ethyl	
	or	
	isopropyl	
	JO.	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	

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pyl ropyl utyl ropyl utyl ropyl ropyl ropyl	Zı	R ⁴⁴
pyl ropyl utyl copyl rtyl rtyl rtyl rtyl	methyl	carboxamidobuty1-2-
pyl ropyl ropyl ropyl ropyl ropyl ropyl	or	y1
oyl ropyl ropyl ropyl ropyl ropyl ropyl ropyl	ethyl	
pyl ropyl ropyl ropyl rtyl ryl ryl ryl ryl	or	
ropyl utyl ropyl ropyl ropyl ropyl	isopropyl	
ropyl utyl ropyl ropyl atyl copyl	or	
utyl copyl atyl copyl ityl ityl	cyclopropyl	
utyl copyl atyl copyl ityl ityl	or	
pyl ropyl ltyl syl ropyl	cyclobutyl	
eopyl atyl atyl copyl copyl atyl atyl atyl	or	
pyl ropyl syl ropyl ropyl	phenyl	
pyl tcopyl tyl copyl tryl	methyl	isobutyramido
pyl rcpyl ltyl copyl	or	
yyl tryl yyl copyl	ethyl	
9y1 try1 try1 sy1 ropy1	or	
ropyl tryl pyl copyl	isopropyl	
ropyl atyl pyl copyl ropyl ropyl atyl	or	
utyl yyl copyl	cyclopropyl	
utyl yyl copyl	or	
oyl copyl atyl	cyclobutyl	
oyl copyl atyl	or	
oyl copyl utyl	phenyl	
or ethyl or isopropyl or cyclopropyl or cyclobutyl or phenyl	methyl	isobutoxy
ethyl or isopropyl or cyclopropyl or cyclobutyl or phenyl	or	
or isopropyl or cyclopropyl or cyclobutyl or phenyl	ethyl	
isopropyl or cyclopropyl or cyclobutyl or phenyl	or	
or cyclopropyl or cyclobutyl or phenyl	isopropyl	
cyclopropyl or cyclobutyl or phenyl	or	
or cyclobutyl or phenyl	cyclopropyl	
cyclobutyl or phenyl	or	
or phenyl	cyclobutyl	
phenyl	or	
	phenyl	

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Core	$\mathbf{z_i}$	R**
Triazinone	methyl	carboethoxy
	or	
	ethy1	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
•	or	
	phenyl	
Triazinone	methyl	carboxyl
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Triazinone	methyl	amino
	or	
	ethy1	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	

1

hydroxy

methyl

Core Azaquinone ethyl or

isopropyl or cyclopropyl

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carboxamidobutyl-2-yl carboxamidobenzyl isobutyramido cyclopropyl or cyclobutyl or or
isopropyl
or
cyclopropyl
or
phenyl
methyl
or
isopropyl
or
cyclopropyl
or
isopropyl
or
cyclopropyl
or
cyclopropyl
or
cyclopropyl
or methyl
or
ethyl
or
isopropyl
or methyl phenyl or ethyl Azaquinone Azaquinone Core Azaquinone

isobutylsulfonyl

Azaquinone

or cyclobutyl or phenyl methyl or lsopropyl or cyclopropyl or cyclobutyl or

trifluoromethyl

Azaquinone

methyl
or
ethyl
or
isopropyl
or
cyclopropyl

cyclobutyl or phenyl

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ž. carboethoxy isobutoxy carboxyl methyl
or
ethyl
or
isopropyl
or
cyclobutyl
or
phenyl
methyl
or
isopropyl
or
cyclobutyl
or
phenyl
or
ethyl
or
cyclobutyl
or
cyclobutyl
or
phenyl
or
cyclobutyl
or
cyclobutyl
or
phenyl
or
cyclobutyl
or
phenyl
or
cyclobutyl
or
phenyl
or
phenyl
or
cyclobutyl
or
phenyl
or
phenyl
or
phenyl
or
phenyl
or
cyclobutyl
or
phenyl
or Azaquinone Core Azaquinone Azaquinone

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Core	$\mathbf{z}_{_{1}}$	R ⁴⁴
Azaquinone	methyl	amino
	or .	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Pyrazinone	methyl	hydroxy
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Pyrazinone	methyl	isobutyleulfonyl
	or	
	ethyl	
	or	
	isopropyl	
	or	
-	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	

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Core	Z,	R**
yrazinone	methy1	trifluoromethyl
ŕ	or	
٠	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Pyrazinone	methyl	carboxamidobenzyl
	or	-
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Pyrazinone	methyl	carboxamidobuty1-2-
,	or	yl
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	

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Core	\mathbf{z}_{i}	R ⁴⁴
Pyrazinone	methyl	isobutyramido
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Pyrazinone	methyl	isobutoxy
	or	
	ethyl	
	or	
	isopropyl	
	or	. •
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Pyrazinone	methyl	carboethoxy
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	

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carboxyl hydroxy amino methyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
ethyl
or
isopropyl
or
cyclobutyl
or
ethyl
or
isopropyl
or
cyclobutyl
or
isopropyl
or
cyclobutyl
or
isopropyl
or
cyclobutyl
or
cyclobutyl Isoxazinone Pyrazinone Core Pyrazinone

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Core	2,	R44
Isoxazinone	methyl	isobutylsulfonyl
	or	
	ethyl	
	or	
	isopropyl	
	or.	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	pheny1	
Isoxazinone	methyl	trifluoromethyl
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
-	cyclobutyl	
	or	
	phenyl	
Isoxazinone	methy1	carboxamidobenzyl
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	

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Core	$\mathbf{z_1}$	R ⁴⁴
Isoxazinone	methyl	carboxamidobutyl-2-
	or	yı
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	-
	or	
	phenyl	
Isoxazinone	methyl	isobutyramido
	or	
	ethyl	
	or	
	isopropyl	
	·	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	-
Isoxazinone	methyl	isobutoxy
	or	
	ethyl	
	. zo	-
	lsopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	

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Core	$\mathbf{z_i}$	R ⁴⁴
Isoxazinone	methyl	carboethoxy
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Isoxazinone	methyl	carboxyl
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	٠
	or	
	phenyl	
Isoxazinone	methyl	amino
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	

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1sobutylsulfonyl trifluoromethyl , E hydroxy methyl
or
ethyl
or
lsopropyl
or
cyclopropyl or cyclopropyl or cyclobutyl or phenyl cyclopropyl or cyclobutyl or cyclobutyl or or isopropyl or methyl
or
ethyl
or
lsopropyl or phenyl phenyl methyl ethyl Dihydrotriazine dione Dihydrotriazine dione Dihydrotriazine dione

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carboxamidobutyl-2-yl carboxamidobenzyl isobutyramido methyl
or
ethyl
or
isopropyl
or
cyclopropyl
or isopropyl
or
cyclopropyl
or isopropyl
or
cyclopropyl
or
cyclobutyl
or
or cyclobutyl or phenyl cyclobutyl or phenyl methyl or methyl ethyl or ethyl or Dihydrotriazine dione Dihydrotriazine dione Dihydrotriazine dione

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isobutoxy

methyl

Dihydrotriazine dione

Core

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isobutylsulfonyl , ; hydroxy amino cyclopropyl
or
cyclobutyl
or
phenyl methyl
or
ethyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or ethyl or 1sopropyl or methyl or phenyl methyl Dihydrotriazine dione Core Pyridine Pyridine

carboethoxy

cyclopropyl

isopropyl

ethyl or

or cyclobutyl or

phenyl

Dihydrotriazine dione

methyl
or
ethyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
cyclobutyl

or
ethyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or

Dihydrotriazine dione

carboxyl

methyl

or ethyl or

isopropyl
or
cyclopropyl
or
cyclobutyl
or

phenyl

į	777
1	:
•	_

carboxamidobutyl-2-yl carboxamidobenzyl trifluoromethyl phenyl
methyl
or
ethyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
cyclobutyl or isopropyl or cyclopropyl or cyclobutyl or phenyl cyclopropyl or cyclobutyl or or isopropyl or methyl or ethyl methyl ethyl Core Pyridine Pyridine Pyridine

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isobutyramido carboethoxy isobutoxy methyl
or
isopropyl
or
cycloputyl
or
phenyl
methyl
or
ethyl
or
isopropyl
or
cycloputyl
or
cyclobutyl
or
ethyl
or
isopropyl
or
isopropyl
or
or
isopropyl
or
or
or
phenyl methyl
or
ethyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
cyclobutyl
or Core Pyridine Pyridine Pyridine

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Core Pyridine

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	i i	400	_	7.	294
21	K			ī	4
methyl	carboxyl	Pyridine	em —	methyl	isobutylsulfonyl
or			, o		
ethyl		-	e et	ethyl	
or			or		
isopropyl			- Bi	isopropyl	
or			or		
cyclopropyl			ַל	cyclopropyl	
or			or		
cyclobutyl			<u>δ</u>	cyclobutyl	
or			or		
phenyl			ųď	phenyl	
methyl	amino	Pyridine	ш	methyl	trifluoromethyl
or			or		
ethyl			e et	ethyl	
o io			or	•	
isopropy1			18	isopropyl	
or			or		
cyclopropyl			<u>\forall 1</u>	cyclopropyl	
or			or		
cyclobutyl			<u>tr</u>	cyclobutyl	
or			or		
phenyl	-		hq	phenyl	
methyl	hydroxy	Pyridine	me	methyl	carboxamidobenzyl
or			o Po	•	
ethyl			et	ethyl	
or			or		
sopropyl			i.e	isopropyl	
or .			or		
cyclopropyl			<u>ਨੇ</u>	cyclopropyl	
or			P		
cyclobutyl			70	cyclobutyl	•
or			o o	_	
phenyl			ηά	phenyl	

Pyridine

;	7
	77.
	>

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Core	$\mathbf{z}_{_{1}}$	R ⁴⁴
Pyridine	methyl	carboxamidobutyl-2-
	or	yl
	ethyl	
	or	
1	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Pyridine	methyl	isobutyramido
	or	
	ethyl	
	or	
	isopropyl	
,	or	
	cyclopropyl	-
	or	
	cyclobutyl	
	or	
	phenyl	
Pyridine	methyl	isobutoxy
	or	
	ethyl	
	or	
	isopropyl	
	or .	
	cyclopropyl	
	io.	
	cyclobutyl	
	or	
. —	phenyl	

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Core	2,	R**
Pyridine	methyl	carboethoxy
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Pyridine	methyl	carboxyl
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or .	
	phenyl	
Pyridine	methyl	amino
	or	
	ethyl	
	or	
	1sopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	

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1sobutyleulfonyl trifluoromethyl π**.** hydroxy methyl
or
ethyl
or
lsopropyl
or
cyclopropyl or
cyclobutyl
or
phenyl
methyl
or
ethyl
or
isopropyl
or
cyclobropyl
or
cyclobutyl
or or cyclopropyl cyclobutyl ethyl or isopropyl methyl or or phenyl Core Pyrazine Pyrazine Pyrazine

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carboxamidobutyl-2-yl carboxamidobenzyl isobutyramido isopropyl or cyclopropyl or methyl
or
ethyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
cyclobutyl
or methyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
phenyl
methyl
or cyclobutyl or phenyl Core Pyrazine Pyrazine Pyrazine

ž,

Core

Pyrazine

isobutoxy

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Core	Z,	R ⁴⁴
Pyrazine	methyl	amino
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Pyrimidine	methyl	hydroxy
	or	
·,	ethy1	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
-	or	
	phenyl	
Pyrimidine	methyl	isobutylsulfonyl
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	

carboethoxy

Pyrazine

methyl
or
isopropyl
or
cyclobutyl
or
cyclobutyl
or
phenyl
methyl
or
isopropyl
or
cyclobutyl
or
isopropyl
or
isopropyl
or
cyclobutyl
or
phenyl
or
cyclobutyl
or
cyclobutyl
or
phenyl

carboxyl

Pyrazine

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carboxamidobutyl-2-yl carboxamidobenzyl trifluoromethyl methyl
or
isopropyl
or
cyclopropyl
or
phenyl
methyl
or
ethyl
or
isopropyl
or
cyclobutyl
or
cyclobutyl
or
isopropyl
or
isopropyl
or
isopropyl
or
or
isopropyl
or
or
isopropyl
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isopropyl
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isopropyl
or
isopropyl
or
isopropyl
or
isopropyl
or
or
isopropyl
or
isopropyl
or
or
isopropyl
or
or
isopropyl
or
or
or or cyclopropyl or cyclobutyl or methyl or ethyl or isopropyl phenyl Pyrimidine Pyrimidine Core Pyrimidine

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Core	. 'Z	R ⁶⁴
Pyrimidine	methyl	isobutyramido
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
•	cyclobutyl	
	or	
	phenyl	
Pyrimidine	methyl	isobutoxy
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Pyrimidine	methyl	carboethoxy
	or	
	ethyl	
	or	
	1sopropy1	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	й .	
	phenyl	

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74 14 carboxyl hydroxy amino methyl
or
ethyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or methyl
or
ethyl
or
isopropyl
or
cyclopropyl.
or
cyclobutyl
or
phenyl methyl
or
ethyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
phenyl Pyrimidine Core Pyrimidine Triazine

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Core	Z,	R ⁴⁴
Triazine	methyl	isobutylsulfonyl
	or .	
	ethyl	•
	or	
	isopropyl	
	or	
-	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Triazine	methyl	trifluoromethyl
	or	
	ethyl	
	or	
-	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Triazine	methyl	carboxamidobenzyl
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	

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carboxamidobutyl-2-yl isobutyramido R44 isobutoxy methyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
cyclobutyl
or methyl
or
ethyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
phenyl methyl
or
ethyl
or
isopropyl
or
cyclopropyl
or
cyclobutyl
or
cyclobutyl
or
phenyl 7 Core Triazine Triazine Triazine

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Core	$\mathbf{z_i}$	R ⁴⁴
Triazine	methyl	carboethoxy
	or	
	ethyl	
	or	
	isopropyl	
	or	,
	cyclopropyl	
	or	
	cyclobutyl	
	or	
	phenyl	
Triazine	methyl	carboxyl
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
•	cyclobutyl	
	or	
i	phenyl	
Triazine	methyl	amino
	or	
	ethyl	
	or	
	isopropyl	
	or	
	cyclopropyl	
	or	
•	cyclobutyl	
	or	
	phenyl	

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The generic terms described below are applicable soley for compounds based upon Formula A. Therefore, these generic terms, unless otherwise indicated or generally known in the art, should not be utilized to construe the meaning of compounds represented by general Pormula I.

The terms "hydrocarbon" and "hydrocarbyl" as used herein in connection with Formula A describe organic compounds or radicals consisting exclusively of the elements carbon and hydrogen. These moieties include alkyl, alkenyl, alkynyl, and aryl moieties also include alkyl, alkenyl, alkynyl, and aryl moieties substituted with other aliphatic or cyclic hydrocarbon groups, such as alkaryl, alkenaryl and alkynaryl. Unless otherwise indicated, these moieties preferably comprise 1 to 20 carbon atoms.

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The "substituted hydrocarbyl" moieties described herein in connection with Formula A are hydrocarbyl moieties which are substituted with at least one atom other than carbon, including moieties in which a carbon chain atom is substituted with a hetero atom such as nitrogen, oxygen, silicon, phosphorous, boron, sulfur, or a halogen atom. Exemplary substituted hydrocarbyl moieties include, heterocyclo, alkoxyalkyl, aryloxyalkyl, alkynyloxyalkyl, aryloxyalkyl, hydroxyalkyl, protected hydroxyalkyl, keto, acyl, nitroalkyl, aminoalkyl, cyano, alkylthioalkyl, arylthioalkyl, ketals, acetals, amides, acids, esters and the like.

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The term "heteroatom" described herein in connection with Formula A shall mean atoms other than carbon and hydrogen.

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The term "physiological conditions" are those as characteristic of or approrpriate to an organisms (to a human beings) healthy or normal functioning in those organism (i.e., body) parts having its intracellular and

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its extracellular fluids.

Unless otherwise indicated, the alkyl groups described herein in connection with Formula A are preferably lower alkyl containing from one to eight carbon atoms in the principal chain and up to 20 carbon atoms. They may be straight or branched chain or cyclic and include methyl, ethyl, propyl, isopropyl, butyl, hexyl and the like.

Unless otherwise indicated, the alkenyl groups described herein in connection with Formula A are preferably lower alkenyl containing from two to eight carbon atoms in the principal chain and up to 20 carbon atoms. They may be straight or branched chain or cyclic and include ethenyl, propenyl, isopropenyl, butenyl, isobutenyl, hexenyl, and the like.

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Unless otherwise indicated, the alkynyl groups described herein in connection with Formula A are preferably lower alkynyl containing from two to eight carbon atoms in the principal chain and up to 20 carbon atoms. They may be straight or branched chain and include ethynyl, propynyl, butynyl, isobutynyl, hexynyl, and the like.

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The terms "aryl" or "ar" as used herein in connection with Formula A alone or as part of another group denote optionally substituted homocyclic aromatic groups, preferably monocyclic or bicyclic groups containing from 6 to 12 carbons in the ring portion, such as phenyl, biphenyl, naphthyl, substituted phenyl, substituted phenyl, substituted aryll and substituted phenyl are the more preferred aryl.

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The terms "halogen" or "halo" as used herein in connection with Formula A alone or as part of another group refer to chlorine, bromine, fluorine, and iodine.

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The terms "heterocyclo" or "heterocyclic" as used herein in connection with Formula A alone or as part of another group denote optionally substituted, fully

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heterocyclo, and R² is hydrogen, hydrocarbyl or hydrocarbyl, heterosubstituted hydrocarbyl, substituted hydrocarbyl. The heterocyclo group preferably has heteroatom in at least one ring, and preferably 5 or 6 aromatic or nonaromatic groups having at least one saturated or unsaturated, monocyclic or bicyclic,

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an acyl group as described above bonded through an oxygen with Formula A alone or as part of another group, denotes linkage (-0-), e.g., RC(0)0- wherein R is as defined in The term "acyloxy," as used herein in connection connection with the term "acyl." S

the invention. Pharmaceutically acceptable sales of such tautomeric, geometric or stereoisomeric forms are also geometric isomers, R- and S-enantiomers, diastereomers, other mixtures thereof, as falling within the scope of d-isomers, 1-isomers, the racemic mixtures thereof and including cis- and trans-geometric isomers, E- and Z-Compounds of the present invention can exist in tautomeric, geometric or stereoisomeric forms. The present invention contemplates all such compounds, included within the invention.

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remainder of the molecule through a carbon or heteroatom.

Exemplary heterocyclo include heteroaromatics such as

1 or 2 oxygen atoms, 1 or 2 sulfur atoms, and/or 1 to 4

atoms in each ring.

nitrogen atoms in the ring, and may be bonded to the

substituents include one or more of the following groups:

hydrocarbyl, substituted hydrocarbyl, keto, hydroxy,

protected hydroxy, acyl, acyloxy, alkoxy, alkenoxy,

quinolinyl, or isoquinolinyl and the like. Exemplary

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furyl, thienyl, pyridyl, oxazolyl, pyrrolyl, indolyl,

alkynoxy, aryloxy, halogen, amido, amino, nitro, cyano,

thiol, ketals, acetals, esters and ethers.

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same side of the double bond ("cis") or on opposite sides geometric isomerism in which two carbon atoms connected by a double bond will each have a hydrogen atom on the The terms "cis" and "trans" denote a form of of the double bond ("trans").

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preferably 5 or 6 atoms in each ring. The heteroaromatic

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group preferably has 1 or 2 oxygen atoms, 1 or 2 sulfur

atoms, and/or 1 to 4 nitrogen atoms in the ring, and may

be bonded to the remainder of the molecule through a

carbon or heteroatom. Exemplary heteroaromatics include

having at least one heteroatom in at least one ring, and

connection with Formula A alone or as part of another

The term "heteroaromatic" as used herein in

group denote optionally substituted aromatic groups

groups, and are meant to include both cis and trans or Some of the compounds described contain alkenyl "E" and "Z" geometric forms.

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substituents include one or more of the following groups:

hydrocarbyl, substituted hydrocarbyl, keto, hydroxy,

protected hydroxy, acyl, acyloxy, alkoxy, alkenoxy,

quinolinyl, or isoquinolinyl and the like. Exemplary furyl, thienyl, pyridyl, oxazolyl, pyrrolyl, indolyl,

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Formula A alone or as part of another group, denotes the

The term "acyl," as used herein in connection with

alkynoxy, aryloxy, halogen, amido, amino, nitro, cyano,

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chiol, ketals, acetals, esters and ethers.

group -COOH of an organic carboxylic acid, e.g., RC(0)-,

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wherein R is hydrogen, R1, R10-, R1R2N-, or R1S-, R1 is

molety formed by removal of the hydroxyl group from the

stereocenters and are meant to include R, S, and mixtures Some of the compounds described contain one or more of R and S forms for each stereocenter present.

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principally in the "keto" form and in part or principally group present. Compounds of the present invention having combinations thereof alone or as part of a heterocyclic ring system. Such carbonyl groups may exist in part or as one or more "enol" forms of each aldehyde and ketone Some of the compounds described herein may contain one or more ketonic or aldehydic carbonyl groups or

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aldehydic or ketonic carbonyl groups are meant to include both "keto" and "enol" tautomeric forms. Some of the compounds described herein may contain one or more amide carbonyl groups or combinations thereof alone or as part of a heterocyclic ring system. Such carbonyl groups may exist in part or principally in the "keto" form and in part or principally as one or more "enol" forms of each amide group present. Compounds of the present invention having amidic carbonyl groups are meant to include both "keto" and "enol" tautommeric forms. Said amide carbonyl groups may be both oxo (C=O) and thiono (C=S) in type.

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Some of the compounds described herein may contain one or more imine or enamine groups or combinations thereof. Such groups may exist in part or principally in the "imine" form and in part or principally as one or more "enamine" forms of each group present. Compounds of the present invention having said imine or enamine groups are meant to include both "imine" and "enamine" tautomeric forms.

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The present invention also comprises a treatment and prophylaxis in anticoagulant therapy for the treatment and prevention of a variety of thrombotic conditions including coronary artery and cerebrovascular disease in a subject, comprising administering to the subject having such disorder a therapeutically-effective amount of a compound of Pormula (I or A):

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or a pharmaceutically-acceptable salt thereof.

As a further embodiment, compounds of the present invention of Formula (I or A) or a pharmaceutically-

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acceptable salt thereof as defined above, comprise a treatment and prophylaxis of coronary artery disease, cerebrovascular disease and other coagulation cascade related disorders in a subject, comprising administering to the subject having such disorder a therapeutically-effective amount of compounds of Formula (I or A) of the present invention or a pharmaceutically-acceptable salt

Compounds of the present invention of Formula (I or A) or a pharmaceutically-acceptable salt thereof can also be used whenever inhibition of blood coagulation is required such as to prevent coagulation of stored whole blood and to prevent coagulation in other biological samples for testing or storage. Thus coagulation inhibitors of the present inhibition can be added to or contacted with stored whole blood and any medium containing or suspected of containing plasma coagulation factors and in which it is desired that blood coagulation be inhibited, e.g. when contacting the mammal's blood with material selected from the group consisting of vascular grafts, stents, orthopedic prothesis, cardiac prosthesis, and extracorporeal circulation systems.

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Compounds of Formula (I or A) are capable of inhibiting activity of serine proteases related to the coagulation cascade, and thus could be used in the manufacture of a medicament, a method for the prophylactic or therapeutic treatment of diseases mediated by coagulation cascade serine proteases, such as inhibiting the formation of blood platelet aggregates, inhibiting the formation of fibrin, inhibiting thrombus formation, and inhibiting embolus formation in a mammal, in blood, in blood products, and in mammalian organs. The compounds also can be used for treating or preventing unstable angina, refractory angina, myocardial infarction, transient ischemic attacks, atrial

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fibrillation, thrombotic stroke, embolic stroke, deep

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methods. The compounds of Formula (I or A) would be also coagulation cascade serine proteases to enable the design ocular build up of fibrin, and reocclusion or restenosis useful in prevention of cerebral vascular accident (CVA) vein thrombosis, disseminated intravascular coagulation, of recanalized vessels in a mammal. The compounds also of better inhibitors and development of better assay can be used to study the mechanism of action of or stroke.

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norganic acid or from an organic acid. Examples of such Suitable pharmaceutically-acceptable base addition salts neterocyclic, carboxylic and sulfonic classes of organic Also included in the family of compounds of Formula the nature of the salt is not critical, provided that it of compounds of Formula (I or A) include metallic salts embraces salts commonly used to form alkali metal salts acids, examples of which are formic, acetic, propionic, and to form addition salts of free acids or free bases. citric, ascorbic, glucoronic, maleic, fumaric, pyruvic, succinic, glycolic, gluconic, lactic, malic, tartaric, lydrolodic, nitric, carbonic, sulfuric and phosphoric ncid. Appropriate organic acids may be selected from octassium, sodium and zinc or organic salts made from The term "pharmaceutically-acceptable salt" salicylic, p-hydroxybenzoic, phenylacetic, mandelic, syclohexylaminosulfonic, algenic, galacturonic acid. (I or A) are the pharmaceutically-acceptable salts pharmaceutically-acceptable acid addition salts of compounds of Formula (I or A) may be prepared from aspartic, glutamic, benzoic, anthranilic, mesylic, liphatic, cycloaliphatic, aromatic, araliphatic, embonic (pamoic), methanesulfonic, ethylsulfonic, nade from aluminum, calcium, lithium, magnesium, Inorganic acids are hydrochloric, hydrobromic, is pharmaceutically acceptable. Suitable benzenesulfonic, sulfanilic, stearic,

the appropriate acid or base with the compound of Formula methylglucamine) and procain. All of these salts may be N, N'-dibenzylethyleneldiamine, choline, chloroprocaine, compound of Formula (I or A) by reacting, for example, prepared by conventional means from the corresponding diethanolamine, ethylenediamine, meglumine (N-(I or A).

association with at least one pharmaceutically-acceptable desired, other active ingredients. The active compounds active compounds of Formula (I or A) in association with pharmaceutical composition comprising a therapeuticallypharmaceutical composition adapted to such a route, and carriers and/or diluents and/or adjuvants (collectively compositions of the present invention can comprise the of the present invention may be administered by any referred to herein as "carrier" materials) and, if one or more non-toxic, pharmaceutically-acceptable effective amount of a compound of Formulas (I) in in a dose effective for the treatment intended. carrier, adjuvant or diluent. Pharmaceutical suitable route, preferably in the form of a The present invention also comprises a

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oculary, or topically. For treating ocular build up of fibrin, the compounds may be administered intraocularly intraperitoneally, subcutaneously, intramuscularly, The active compounds and composition may, for example, be administered orally, intravascularly, or topically as well as orally or parenterally.

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The active ingredient The compounds can be administered in the form of a can be compressed into pellets or small cylinders and materials such as biodegradable polymers or synthetic formulated in such a manner as to permit a sustained implanted subcutaneously or intramusculary as depot depot injection or implant preparation which may be injections or implants. Implants may employ inert release of the active ingredient.

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silicones, for example, Silastic, silicone rubber or other silicon containing polymers.

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The compounds can also be administered in the form of liposome delivery systems, such as small unilamellar vesicles, large unilamellar vesicles and multilamellar vesicles. Liposomes can be formed from a variety of phospholipids, such as cholesterol, stearylamine or phosphatidylcholines.

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polycyanoacrylates and cross linked or amphitpathic block monoclonal antibodies as individual carriers to which the compound molecules are coupled. The compounds may also substituted with palmitoyl residues. Furthermore, the The compounds may also be delivered by the use of drug, for example, polylactic acid, polyglycolic acid, polymers useful in achieving controlled release of a compounds may be coupled to a class of biodegradable be coupled with soluble polymers as targetable drug aspartamide-phenol, or ployethyleneoxide-polylysine polyepsilon caprolactone, polyhydroxy butyric acid, polyvinylpyrrolidone, pyran copolymer, polyhydroxypolyorthoesters, polyacetals, polydihydropyrans, propyl-methacrylamide-phenol, polyhydroxyethylcopolymers of polylactic and polyglycolic acid, carriers. Such polymers can include copolymers of hydrogels.

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For oral administration, the pharmaceutical composition may be in the form of, for example, tablets, capsules (each of which includes sustained release or timed release formulations), pills, powders, granules, elixers, tinctures, suspensions, liquids including syrups, and emulsions. The pharmaceutical composition is preferably made in the form of a dosage unit containing a particular amount of the active ingredient. Examples of such dosage units are tablets or capsules. The active ingredient may also be administered by injection as a composition wherein, for example, saline, dextrose or

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water may be used as a suitable carrier.

The amount of therapeutically active compounds which are administered and the dosage regimen for treating a disease condition with the compounds and/or compositions of this invention depends on a variety of factors, including the age, weight, sex and medical condition of the subject, the severity of the disease, the route and frequency of administration, and the particular compound employed, and thus may vary widely.

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The pharmaceutical compositions may contain active ingredients in the range of about 0.1 to 2000 mg, and preferably in the range of about 0.5 to 500 mg. A daily dose of about 0.01 to 100 mg/kg body weight, and preferably between about 0.5 and about 20 mg/kg body weight, may be appropriate. The daily dose can be administered in one to four doses per day.

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The compounds may be formulated in topical ointment or cream, or as a suppository, containing the active ingredients in a total amount of, for example, 0.075 to 30% w/w, preferably 0.2 to 20% w/w and most preferably 0.4 to 15% w/w. When formulated in an ointment, the active ingredients may be employed with either paraffinic or a water-miscible ointment base.

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Alternatively, the active ingredients may be formulated in a cream with an oil-in-water cream base. If desired, the aqueous phase of the cream base may include, for example at least 30% w/w of a polyhydric alcohol such as propylene glycol, butane-1,3-diol, mannitol, sorbitol, glycerol, polyethylene glycol and mixtures thereof. The topical formulation may desirably include a compound which enhances absorption or penetration of the active ingredient through the skin or other affected areas. Examples of such dermal penetration enhancers include dimethylsulfoxide and related analogs. The compounds of this invention can also be administered by a transdermal device. Preferably

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mucosa of the recipient. If the active agent is absorbed topical administration will be accomplished using a patch either of the reservoir and porous membrane type or of a through the skin, a controlled and predetermined flow of permeable adhesive, which is in contact with the skin or solid matrix variety. In either case, the active agent microcapsules through a membrane into the active agent the active agent is administered to the recipient. In the case of microcapsules, the encapsulating agent may is delivered continuously from the reservoir or also function as the membrane.

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emulsifier with a fat or an oil or with both a fat and an Span 80, cetostearyl alcohol, myristyl alcohol, glyceryl stabilizer(s) make-up the so-called emulsifying wax, and stabilizer. It is also preferred to include both an oil Together, the emulsifier(s) with or without dispersed phase of the cream formulations. Emulsifiers oil. Preferably, a hydrophilic emulsifier is included formulation of the present invention include Tween 60, monostearate, and sodium lauryl sulfate, among others. The oily phase of the emulsions of this invention together with a lipophilic emulsifier which acts as a called emulsifying ointment base which forms the oily emulsifier, it may comprise a mixture of at least one the wax together with the oil and fat make up the somay be constituted from known ingredients in a known and emulsion stabilizers suitable for use in the While the phase may comprise merely an and a fat.

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in most oils likely to be used in pharmaceutical emulsion product with suitable consistency to avoid leakage from properties, since the solubility of the active compound tubes or other containers. Straight or branched chain, formulation is based on achieving the desired cosmetic preferably be a non-greasy, non-staining and washable formulations is very low. Thus, the cream should The choice of suitable oils or fats for the

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blend of branched chain esters may be used. These may be fatty acids, isopropyl myristate, decyl oleate, isopropyl required. Alternatively, high melting point lipids such used alone or in combination depending on the properties as white soft paraffin and/or liquid paraffin or other isocetyl stearate, propylene glycol diester of coconut palmitate, butyl stearate, 2-ethylhexyl palmitate or a mono- or dibasic alkyl esters such as diisoadipate, mineral oils can be used.

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sodium chloride, and/or various buffers. Other adjuvants esters, talc, stearic acid, magnesium stearate, magnesium Such capsules or tablets may contain a controlled-release administration. The compounds may be dissolved in water, polyethylene glycol, propylene glycol, ethanol, corn oil, and modes of administration are well and widely known in the present invention are ordinarily combined with one or polyvinylpyrrolidone, and/or polyvinyl alcohol, and then formulation as may be provided in a dispersion of active compound in hydroxypropylmethyl cellulose. Formulations cottonseed oil, peanut oil, sesame oil, benzyl alcohol, granules having one or more of the carriers or diluents tableted or encapsulated for convenient administration. If administered per os, the compounds For therapeutic purposes, the active compounds of sulfuric acids, gelatin, acacia gum, sodium alginate, more adjuvants appropriate to the indicated route of may be admixed with lactose, sucrose, starch powder, for parenteral administration may be in the form of suspensions may be prepared from sterile powders or cellulose esters of alkanoic acids, cellulose alkyl aqueous or non-aqueous isotonic sterile injection oxide, sodium and calcium salts of phosphoric and These solutions and mentioned for use in the formulations for oral solutions or suspensions. the pharmaceutical art. administration.

In practicing the methods of the present invention

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Typical doses of coagulation cascade inhibitors of

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restenosis), anti-coagulants such as aspirin, warfarin or lowering agents including antihypercholesterolemics (e.g. cerebrovascular disease, the compounds and pharmaceutical combination with other therapeutics or in vivo diagnostic suitable anti-platelet agreggation agents, including, but receptor antagonists (e.g. to treat or prevent unstable drugs, or other cardiovascular agents (loop diuretics angina or to prevent reocculsion after angioplasty and effects in the treatment of various pathologies, lipid compositions of the present invention are administered ovastatin, simvastatin, pravastatin, and fluvastatin, epoxymexlerenone), angiotensin converting enzyme (e.g. not limited to ticlopidine or clopidrogel, fibrinogen ACE) inhibitors, angiotensin II receptor antagonists, HMG CoA synthatase inhibitors, etc.), anti-diabetic thrombotic conditions including coronary artery and present invention can also be co-administered with activators or streptokinase to achieve synergistic The coagulation cascade inhibitors of the heparins, thrombolytic agents such as plasminogen HMG CoA reductase inhibitors such as mevastatin, for the treatment and prevention of a variety of alone or in combination with one another, or in chiazide type diuretics, nitrates, aldosterone intagonistics (i.e., spironolactone and agents.

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thrombolytic agents, depending on a patient's therapeutic administered without coadministration of additional anticascade inhibitors administered without coadministration platelet agents, anticoagulation agents, cardiovascular the present invention with other suitable anti-platelet compounds which selectively inhibit human TF-VIIA over VIIA inhibition over both human Thrombin II and human therapeutic agents, or thrombolytic agents, or may be therapeutic agents, or thrombolytic agents may be the same as those doses of coagulation cascade inhibitors of additional anti-platelet agents, anticoagulation substantially less than those doses of coagulation The present novel methods preferably employ agents, anticoagulation agents, cardiovascular agents, cardiovascular therapeutic agents, or needs. 20 15 2

Preferably, the compounds have a human TF-VIIA IC, of the inhibition of both human Thrombin II and human factor less than 0.5 mM and also have a selectivity ratio of TFat least 100. Even more preferably, the compounds have a factor Xa inhibition of at least 10, and more preferably selectivity ratio of TF-VIIA inhibition over both human Thrombin II and human factor Xa inhibition of at least human IF-VIIA IC50 of less than 0.1 mM and also have a 1000, and most preferably at least 10,000.

All mentioned references are incorporated by reference as if here written.

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beta-blockers, antiarrythmics, anti-hypertension agents,

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atheriosclerosis. For example, patients suffering from

and calcium channel blockers) to treat or prevent

coronary artery disease, and patients subjected to

angioplasty procedures, would benefit from

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coagulation cascade inhibitors of the present invention.

Also, coagulation cascade inhibitors could enhance the

efficiency of tissue plasminogen activator-mediated

thrombolytic reperfusion.

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coadministration of fibrinogen receptor antagonists and

following examples are provided to illustrate the present embodiments are not to be construed as limitations. The respect to specific embodiments, the details of these thereof. Without further elaboration, it is believed that one skilled in the art can, using the preceding Although this invention has been described with descriptions, utilize the present invention to its Invention and are not intended to limit the scope

also contemplated. Those skilled in the art will readily illustrated in the schemes or the following Examples are processes of the following preparative procedures can be disclosure in any way whatsoever. Compounds containing illustrative and not limitative of the remainder of the understand that known variations of the conditions and multiple variations of the structural modifications fullest extent. Therefore the following preferred specific embodiments are to be construed as merely used to prepare these compounds.

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One skilled in the art may use these generic methods the methods of preparation of compounds of Formula (I or and are presented for illustrative purposes only and are invention. All parts are by weight and temperatures are These compounds also may be formed in vivo. the following examples contain detailed descriptions of to prepare the following specific examples, which have These detailed descriptions fall within the scope been or may be properly characterized by ¹H NMR, mass not intended as a restriction on the scope of the spectrometry, elemental composition, and similar Degrees centigrade unless otherwise indicated.

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bis (diphenylphosphino) -1,1'-binaphthyl, "BnOH" represents The following general synthetic sequences are useful represents butyl, "dba" represents dibenzylidene-acetone, represents dichloromethane or methylene chloride, "DIBAH" acids, "AcCN" represents acetonitrile, "AcOH" represents or "DIBAL" represents diisobutylaluminum hydride, "DMF" in making the present invention. Abbreviations used in the schemes and tables include: "AA" represents amino "DCC" represents 1,3-dicyclohexylcarbodiimide, "DCM" benzyl alcohol, "BnCHO" represents 2-phenylethanal, "BnSO₂Cl" represents benzylsulfonyl chloride, "Boc" represents tert-butyloxycarbonyl, "BOP" represents benzotriazol-1-yl-oxy-tris-(dimethylamino), "bu" acetic acid, "BINAP" represents 2,2'-

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represents tetrabutylammonium fluoride, "TBTU" represents tetrahydrofuran, "TMS" represents trimethylsilyl, "TMSCN" chloroperbenzoic acid, "MW" represents molecular weight, pyridine, "RNH," represents a primary organic amine, "pdimethylsulfoxide, "DPPA" represents diphenylphosphoryl azide", "EDC" represents 1-[3-(dimethylamino)propyl]-3represents a phase transfer catalyst , "py" represents ethylcarbodiimide hydrochloride, "Ex. No." represents 2-(iH-benzotriozole-1-yl)-1,1,3,3-tetramethyl uronium "NMM" represents N-methylmorpholine, "Ph" represents phenyl or aryl, "PHTH" represents a phthaloyl group, represents trimethylsilyl cyanide, and "Cbz" or "Z" tetrafluoroborate, "TEA" represents triethylamine, represents trifluoroacetic acid, "THF" represents TBOH" represents paratoluenesulfonic acid, "TBAF" "pn2" represents 4-nitrobenzyloxy-carbonyl, "PTC" hydroxybenzoltriazole", "LDA" represents lithium represents dimethylformamide, "DMSO" represents fluorenylmethoxycarbonyl, "HOBt" represents diisopropylamide, "MCPBA" represents meta-Example Number, "Fmoc" represents 9-20 15

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GENERAL SYNTHETIC PROCEDURES AND SPECIFIC EXAMPLES

represents benzyloxycarbonyl.

synthesized, for example, according to the following The compounds of the present invention can be

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substitutedmethylpyridine with a nucleophilic amine using chloro-6-substitutedmethylpyridine with ammonia using a palladium catalyzed aryl amination procedure leads to a a palladium catalyzed aryl amination procedure leads to 2-amino-6-substitutedmethylpyridine in which the amino Following the procedure of Scheme 1, treatment of a 2group is unsubstituted. Treatment of a 2-chloro-6-A general synthetic approach to substituted pyridines is shown in Schemes 1 through 6 below. procedures and Schemes given below.

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sulfonylated, for example, to the N-acyl derivative or N-Scheme 1 can be converted to the corresponding 2-amino-5bromopyridine compound of Scheme 2 can be converted to substituted secondary 2-aminopyridine. Alternately, a primary or secondary 2-aminopyridne can be acylated or corresponding acylating and sulfonylating agent in the dicarbonate [(Boc),0] and lithium diisopropylamide in could, when desired, be a secondary amine compound, a primary 2-aminopyridine can be further reacted with a procedure of Scheme 2, a 2-aminopyridine compound of suitable non-protic solvent such as tetrahydrofuran. bromopyridine compound using bromine in acetic acid. the corresponding secondary 2-aminopyridine when an primary amine is used. Alternately, the amine used triacetoxyborohydride to prepare the corresponding presence of an equivalence of base. Following the Following the procedure of Scheme 3, a 2-amino-5bromopyridyl))acetate compound using di-t-butyl hydrazine compound, or a hydroxyamine compound. sulfonyl derivative, respectively, using the the corresponding t-butyl 2-(6-(2-amino-5suitable aldehyde or ketone using sodium

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present invention, is the arylation or heteroarylation of leaving group is replace by an aryl group or a heteroaryl Suitable leaving groups for the reaction include have an acetic acid group or a derivative thereof bonded both beta to the carbon having the acetic acid group and preparation of many of the heterocyclic compounds of the neterocyclic ring with the leaving group will preferably neterocyclic ring. In the product of the reaction, the unsubstituted amino group bonded to a ring atom that is to a ring atom alpha to the bromo and a substituted or suitable leaving group on a sp² hybridized carbon of a chloro, bromo, iodo, methylthio, and triflates. The an intermediate compound characterized by having a A specific synthetic process, useful in the group.

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or heteroaryl becomes bonded to the sp' hybridized carbon at the point at which the boron was attached to the aryl boronates may be substituted or unsubstituted. The aryl compounds can also be used instead of the corresponding generally an aryl boronic acid or an ester of the aryl esters of these boronic acids can be used in the same group that is reacted at the sp2 hybridized carbon is The aryl boronic acid; similarly, heteroaryl boronic acids or manner as aryl boronates. The aryl and heteroaryl or heteroaryl ring. Aryl and heteroaryl organotin gamma to the bromo substituted ring carbon.

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Suitable reaction conditions for carrying out this transformation include:

Pd[P(phenyl),1,, 2M Na,CO,, 60-75°C, dimethoxyethane (DME), H₂O, N₂;

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Pd[P(phenyl),],, CB,CO,, dioxane, 100°C;

Pd[P(phenyl),],, Cu(I)-2-thiophenecarboxylate, 70-75°C, anhydrous THF, argon; and

24-Sn(n-butyl), pd[P(phenyl), 14, LiCl, anhydrous dioxane, 85°C, argon or N₂.

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Cu(I)-2-thiophenecarboxylate (Cu(I)-TC) is normally used carbonate base is normally used in an excess of 1.2 to $2\,$ The organo-palladium (e.g., Pd[P(phenyl),],) compound is tetrahydrofuran. The temperature of the reaction is used catalytically in a ratio of 1 to 40 mole %. normally in the range of from about 50 to 100°C. molar equivalents. Suitable solvents include dimethoxyethane (DME), dioxane, 1-propanol, in a mole % of 110-150.

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having a suitable leaving group on $\ensuremath{\mathrm{sp}}^2$ hybridized carbon Schemes 4 through 6 and Examples 1, 3, 4, 5, 6, 7, 8; 9, 10, 11, 12, 13, and 14 show specific applications preparing the intermediate heterocyclic ring compounds and useful as suitable intermediates in this specific of this specific synthetic process. Procedures for

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. 240 synthetic process are given in the schemes and examples listed above.

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Scheme 2: General Synthesis of Pyridines (continued)

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Br2, AcOH

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Scheme 3: General Synthesis of Pyridines (Continued)

Br2, AcOH

Br2, AcOH

B-CH2-HIV

Br2, AcOH

Br₂, AcOH

B-CO-HIN

B-SO₂-HN

Scheme 4: General Synthesis of Pyridines (Continued)

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protected pyridylacetamide. Removal of the the Cbz-group invention. A t-butyl 2-(6-(2-amino-5-bromopyridyl) acetate catalyzed coupling conditions to afford the corresponding with anhydrous hydrogen chloride in dioxane to remove the standard peptide coupling conditions with various amines. B(OH),) using palladium catalyzed coupling conditions to any of Schemes 4 through 6, to a compound of the present t-butyl ester and any other t-butoxycarbonyl protecting afford the corresponding 5-aryl t-butyl pyridylacetate. introduced in a protected form. For example, a acetic .nvention can be accomplished with hydrobromic acid in prepared in Scheme 3 can be converted, as described in 5-heteroaryl t-butyl pyridylacetate. The 5-aryl or 5acid derivative can be converted to a N-carbobenzyloxy heteroaryl t-butyl pyridylacetate is then deprotected acetic acid or, alternatively, using hydrogen in the groups. The acid resulting can then be coupled under can be reacted with a desired arylborinate (1.e., Q-These amines are typically multi-functional and are heteroarylborinate (i.e., Q-B(OH),) using palladium A t-butyl 2-(6-(2-amino-5-bromopyridyl) acetate to give a desired pyridine compound of the present bromopyridyl) acetate can be reacted with a desired presence of a palladium on carbon catalyst. The Alternately, a t-butyl 2-(6-(2-amino-5-

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1. MCPBA, CHCl, 2. TFA, then ion exchange Q-B(OH)₃ Pd(P(phenyl)₃)₄ 2M Na₂CO₃, DME 1. 30% HBr/AcOH 0.000 Boc,O, McCN, TEA, DMA! 1. HCl, Dioxane 2. NH₂, Q⁵-Q⁵-Cb2, EDC HOBT, TEA

Note: Amino, Thiol and hydroxygroups in Q and other groups will also be prote by Boc derivatives.

protected N-oxide of the pyridylacetamide using a peracid

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compounds. These synthetic schemes are exemplified in

specific examples disclosed herein.

protecting groups in any of several ways provides the

such as meta-chloroperbenzoic acid. Removal of these

pyridinylacetamide compound can then be converted to the

dicarbonate. A t-butyl and t-butoxycarbonyl protected

amino, hydroxy and thiol groups using di-t-butyl

deprotected pyridine compound can be reprotected at its

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Scheme 5: General Synthesis of Pyridines (Continued)

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Scheme 6: General Synthesis of Pyridines (Continued)

Note: Arnino, thiol and hydroxygroups in Q and other groups will also be protected as Boc derivatives.

Scheme 7: Pyran

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Scheme 8: Pyran

Step D: TFA, HCI, Dioxane Step E: DPPA Step F: HCI, Dioxane

Step C: UINSI(CH₃)₂, z₄-COCI NH4OAC, HOAC

(H₃C)₂N

Step B: 80°C (CH₃)₂NCH(CH₃)₃

Step A: f -BuOH, heat

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Scheme 9: Pyran

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Scheme 10: Pyran

CO₂H

Step J: Pd/C, H₂

Step I:

Step J: Pd/C, H₂

новт, EDC

z3-NH2

R4b Z1CO-HN

Step I:

Z₁-HN

Step H: Jones Reagent Acetone, OsO₄

Step H: Jones Reagent Acetone, OsO₄

4b z₁CO-HN

z3-NH2

CONH-Z3

новт, EDC

CONH-23

NaBH₄ Ethanol

Z₁CO-HN

NaBH₄ Ethanol

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CONH-Z3

 z_1 -HN,

CONH-23

 $z_1^{\rm CO-HN'}$

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Scheme 12: Pyran

ÇO2H

2 equiv. H₂ noble metal catalyst

2 equiv. H₂ noble metal catalyst

Z₁SO_Z-HN

Step I: Step J: EDC Pd/C, H₂

Step J: Pd/C, H₂ | = R4a

EDC

Step I:

Z₁SO₂-HN

Z3-NH2

HOBT,

Z3-NHZ новт,

CONH-z3

CONH-23

NaBH4 Ethanol

Z1CH2-HN

NaBH4 Ethanol

Z₁SO₂-HN

conh-z3

Z₁SO₂-HN

CONH-23

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Z1CH2-HN

Example 1

reaction mixture was diluted with diethyl ether (700 ml), washed three times with saturated brine (400 ml), dried butoxide (250 mmol, 24.0 g), and toluene (1500 ml) were over MgSO4, and concentrated in vacuo. Purification by bis(diphenylphosphino)-1,1'-binaphthyl (8.8 mmol, 5.41 added to an oven-dried, nitrogen purged flask and the yielded 17.9 g (62% yield) of EX-1A as a red oil. MS g), palladium acetate (8.9 mmol, 2.0 g), sodium tertreaction heated to 70 °C for five hours. The cooled silica gel chromatography (20% ethyl acetate/hexane) EX-1A) 6-Chloro-2-picoline (176 mmol, 19.3 ml), cyclobutylamine (211 mmol, 15.0 g), (+/-)-2,2'-(ES, m/z) 163 (M+H).

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mixture was extracted with three time dichloromethane (50 minutes while maintaining the temperature at $\sim\!20$ °C with browine (110 mmol, 5.7 ml) in acetic acid (5 ml) over 30 The combined dichloromethane fractions were dried 17.9 g) in acetic acid (50 ml) was added a solution of cooling in a water bath. After 1.5 hours the reaction over MgSO, and concentrated in vacuo to give 25.8 g of was mixed with water (50 ml) and neutralized with 50% EX-1B) To a stirred solution of EX-1A (110 mmol, sodium hydroxide while cooling in a ice bath. The

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(5% dichloromethane/hexane to 10% ethyl acetate/hexane) Purification by silica gel chromatography yielded 18.04 g (67% yield) of EX-1B as a pale yellow oil. MS (ES, m/z) 243 (M+H). yellow oil.

EX-1C) To a stirred solution of EX-1B (30 mmol, 7.25 tetrahydrofuran (200 ml) under nitrogen, cooled to -45 °C (1.5M solution in cyclohexane, 33 mmol, 22 ml). After 1 (23% yield) of EX-1C as a pale yellow oil. MS (ES, m/z) ethyl acetate (200 ml), washed two times with water (50 was added lithium diisopropylamide monotetrahydrofuran chromatography (5% ethyl acetate/hexane) yielded 3.1 g ml) and saturated brine (50 ml), dried over MgSO,, and g) and di-tert-butyldicarbonate (182 mmol, 39.75g) in monotetrahydrofuran (1.5M solution in cyclohexane, 30 ammonium chloride, concentrated in vacuo, mixed with mmol, 20 ml) was added and stirring continued for 30 The reaction was quenched with saturated Purification by silica gel hour, additional lithium diisopropylamide concentrated in vacuo. 443 (M+H). minutев.

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chromatography (30-40% ethyl acetate/hexane) yielded 0.65 ethyl acetate (200 ml), washed with water (50 ml) and two times with saturated brine (50 ml), dried over MgSO,, and g (32% yield) of EX-1D as a yellow oil. MS (ES, m/z) 454 EX-1D) To a stirred mixture of EX-1C (4.5 mmol, 2.0 (2.3 mmol, 2.6 g) in ethylene glycol dimethyl ether (80 g), 3-aminobenzene boronic acid monohydrate (6.9 mmol, hours. The cooled reaction mixture was combined with mmol, 30 ml). The reaction was heated to 60 °C for 7 1.07 g), and tetrakis(triphenylphosphine)palladium(0) ml) under nitrogen was added 2M sodium carbonate (60 concentrated in vacuo. Purification by Bilica gel

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hydrogen chloride in dioxane at ambient temperature for 48 hours. The reaction was concentrated in vacuo. The EX-1E) EX-1D (1.4 mmol, 0.64 g) was mixed with 4N

residue (0.5 g), 1-hydroxybenzotriazole hydrate (1.8 mmol, 0.24 g), and 4-(N- $\,$

Purification by silica gel chromatography (ethyl acetate) were added. The reaction was slowly allowed to warm to mixture was combined with ethyl acetate (75 ml), washed temperature and stirred for 23 hours. The reaction was (0.5 mmol, 0.1 g) and triethylamine (2.4 mmol, 0.33 ml) three times with water (25 ml) and saturated brine (25 yielded 0.28 g (35% yield) of EX-1E as a tan solid. MS benzyloxycarbonylamidino)benzylamine (2.0 mmol, 0.71 g) ethylcarbodiimide hydrochloride (1.8 mmol, 0.34 g) and dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride triethylamine (7.0 mmol, 0.97 ml) were added, and the were stirred under nitrogen in dimethylformamide with cooling in an ice bath. 1-(3-Dimethylaminopropyl)3nl), dried over MgSO4, and concentrated in vacuo. reaction was slowly allowed to warm to ambient cooled in an ice bath and additional 1-(3ambient temperature and stir for 3 hours.

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solid. HRMS calc'd for $C_{25}H_{29}N_6O~(M+H):~429.2403.~Found:\\$ 129.2390. Anal. Calc'd for C25H28N6O+3.0 HCl, 1.5 H2O: C, EX-1E (0.48 mmol, 0.27 g) was stirred with hydrogen bromide, 30 wt. % solution in acetic acid (15 ml), in a nitrogen flushed capped vial at ambient temperature for column of AG 2-X8 ion-exchange resin (chloride form) to yield 0.20 g (73% yield) of the product as a light tan precipitate collected and dried to give 0.28 g of pink .9 hours. Diethyl ether was added, and the resulting Conversion to the hydrogen chloride salt was accomplished by elution (deionized water) through a N, 14.88; Cl, 18.83. Found: C, N, 14.61; Cl, 18.97. H, 5.97; H, 6.07; 53.09;

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(ES, m/z) 563 (M+H).

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Example 2

Example 1 (0.111 mmol, 62.8 mg) in acetonitrile (10 ml) was added triethylamine (0.359 mmol, 50 ml), di-tert-butyldicarbonate (0.261 mmol, 60 ml) and 4-dimethylaminopyridine (0.016 mmol, 2 mg). The reaction was stirred at ambient temperature for 15 hours. The reaction was concentrated in vacuo, mixed with ethylacetate (10 ml), washed with two times water (5 ml) and saturated brine (5 ml), dried over MgSO₄, concentrated in vacuo and the Ex-2A used without further purification.

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The EX-2A residue was dissolved in chloroform (10 ml), cooled in an ice bath and 3-chloroperoxybenzoic acid 64% (0.122 mmol, 33 mg) added and stirring continued for 1 hour. Trifluoroacetic acid (10 ml) was added and stirring continued in an ice bath for 1 hour. The reaction was concentrated in vacuo. Purification by reverse phase HPLC (2-12% acetonitrile/water) and lyophilization gave the product as an off-white solid. Conversion to the hydrogen chloride salt was accomplished by elution (deionized water) through a column of AG 2-X8 ion-exchange resin (chloride form) to yield 31 mg (48% yield) of the product as an off-white solid. HPMS calc'd

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Example 3

N, 14.32; Cl, 14.29.

Following the procedures described in Example 1, (3-Amino-5-methoxycarbonylphenyl) boronic acid (200mg, 0.87mmol) in MeCN (3ml) was added to Boc₂O (0.87ml, 0.87mmol) and Et₃N (0.26ml, 1.8mmol) at room temperature. The reaction mixture was kept stirring at room temperature for 4 hr. Then HCl solution (pH=4, 4ml) was added, the mixture was extracted with EtOAc (3X5ml). The combined EtOAc was then dried and concentrated to yield 260mg oil EX-3A. (Yield: 100%.) MS (ES, m/z) 296.12 (M+H).

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Following procedure the procedure of Example 1 for the coupling of the a boronic acid in amino protected form EX-3A was reacted with 2-[2-[N-[[4-(N-t-butoxycarbonylamino)iminomethylphenyl]methyl]-3-bromo-6-1sopropylamino-pyridinyl]]acetamide to give EX-3B without purification. MS (ES, m/z) 675.34 (M+H).

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EX-3B (200mg) in MeOH/H₂O (2ml/0.4ml) was mixed with

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ZN LiOH (0.37ml, 0.74mmol) at 0°C. The mixture was kept stirring at room temperature for 3 hr. Then additional ZN LiOH (0.2ml, 0.4mmol) was added to the mixture, and the mixture was stirred at room temperature for another 2 hr. Then the solution was acidified to pH 7 by 1N HCl and extracted with EtOAc (3 times with 5ml). Solid EX-3C (80mg) which contained the product (LC/MS checked) was also collected by filtering the solution. Combined EtOAc extracts were then dried with Na,SO, and concentrated to yield 15mg crude solid EX-3C which was used for next reaction. MS (ES, m/z) 661.33 (M+H).

EX-3C was converted using similar procedures to those described in Example 2 to give a 19% yield of the product: HRMS calc'd for $C_{25}H_{28}N_6O_4$ (M+H): 477.2250. Found:

Example 4

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Using procedures similar to those described in

Examples 1 and 3, (3-amino-5-methoxycarbonylphenyl)boronic acid was coupled with 2-[2-[N-[4-(N-t-

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butoxycarbonylamino)iminomethylphenyl]methyl]-3-bromo- 6-isopropylamino-pyridinyl]]acetamide afford 2-[2-[N-[[4-

(N-t-butoxycarbonylamino)iminomethyl-phenyl]methyl]-3-[3amino-5-carbomethoxyphenyl)- 6-isopropylaminopyridinyl]]acetamide (EX-4A) in 70% yield: MS (ES, m/z) 575.29 (M+H).

Using procedures similar to those of Example 2, the N-oxide product was formed in 17% yield from EX-4A: HRMS calc'd for $C_{26}H_{10}N_6O_4$ (M+H): 491.2407. Found: 491.2426. Anal. Calc'd for $C_{26}H_{10}N_6O_4+2.15TFA$, 1.5 H_2O : C, 47.71; H, 4.64; N, 11.01. Found: C, 47.76; H, 4.71; N, 10.96.

Example

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Using procedures similar to those described in Example 1, isopropylamine was used instead of cyclobutylamine and reacted with 2-chloro-6-methylpyridine to give EX-5A in an 81% yield: MS (ES, m/z) 151.12 (M+H).

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Similar procedures were used to convert used instead of cyclobutylamine and reacted with 2-chloro-6-methylpyridine to give EX-5A to used instead of cyclobutylamine and reacted with 2-chloro-6-methylpyridine to give the bromopyridine EX-5B in a yield of 55%. MS (ES, m/z) 229.05 (M+H).

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EX-5B (12g, 0.06mol) in THF (100ml) was cooled to -45°C and LDA (60ml, 0.09mol) was added. After 10min, Boc,O (12g, 0.06ml) in THF (50ml) was added to the solution. After 3 hr, the solution was mixed with water (200ml), concentrated to 200ml, extracted with CH,Cl, (3 x 150ml). The combined CH,Cl, extrracts were then dried, concentrated and purified to yield 12g of oil EX-5C. MS (ES, m/z) 329.10 (M+H).

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EX.5C (5g, 15mmol) in THF (50ml) was cooled to -78°C and LDA (15ml, 23mmol) was added. After 30min, dry ice (3g) was added to the solution. After 3 hr, the solution was added with water (200ml), concentrated to 200ml, basified to pH 9 with saturated aqueous Na,CO,, washed with ether (3x50ml), then acidified to pH 5 with IN HCl, and extracted with CH,Cl; (3x150ml). The combined CH,Cl2 was then dried over Na,SO, and concentrated to yield 4.5g of white solid EX-5D. MS (ES, m/z) 373.09 (M+H).

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stirred in the bath and allowed to slowly warm to ambient 1-hydroxybenzotriazole hydrate (9.1 mmol, 1.23 g,), 4-(Nbenzyloxycarbonylamidino) benzylamine hydrochloride (8.7 temperature for 18 hours. The reaction was diluted with To a stirred solution of EX-5D (6.4 mmol, 2.4 g,), mmol, 3.1 g), and triethylamine (14.3 mmol, 2.0 ml,) in dried over magnesium sulfate, filtered and concentrated dimethylformamide (100 ml) under nitrogen cooled in an ethylcarbodiimide hydrochloride (9.1 mmol, 1.74 g) and water (300 ml) and extracted with ethyl acetate (3x125 ml). The combined organic fractions were washed with dilute hydrochloric acid (3x50 ml), saturated sodium combined acid washes were neutralized with saturated acetate (2x50 ml). These new organic fractions were sodium bicarbonate solution and extracted with ethyl brine washed, combined with previous organic washes, bicarbonate solution (2x50 ml), and brine (50 ml). triethylamine (57.4 mmol, 8 ml). The reaction was ice bath was added 1-(3-dimethylaminopropyl)-3-

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the chloroform fractions washed with brine. The combined dichloromethane (50 ml), washed with 2M sodium carbonate fractions were extracted with chloroform (2x25 ml), and organic fractions were cooled, and the resulting solid (3x50 ml), and brine (50 ml). The combined aqueous collected by vacuum filtration to yield 2.19 g (73% residue mixed with ethyl acetate (300 ml) and

520:522 (M+H). Concentration of the filtrate gave an

additional 0.66 g (22 %).

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yield) of EX-5H as an orange solid.

MS (ES, m/z),

for C18H23N5O2Br (M+H): 420.1035. Found: 420.1046. Anal. reaction was concentrated under a stream of nitrogen and the residue was crystallized from acetonitrile / diethyl orange solid. MS (ES, m/z), 420:422 (M+H). HPMS calc'd Calc'd for C18H2N5O2Br +1.95 TFA, 0.15.5 H2O: C, 40.48; dichloromethane (1 ml) and trifluoroacetic acid (1 ml) ether to yield 28 mg (69 % yield) of EX-51 as a pale H, 3.70; N, 10.70. Found: C, 40.75; H, 3.75; N, was stirred at ambient temperature for 30 minutes. A solution of EX-5H (0.096 mmol, 50 mg) in

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benzyloxyohenyl) boronic acid (0.43 mmol, 99 mg), cesium residue was mixed with ethyl acetate (4 ml), washed with concentrated under a nitrogen stream and purification by ethylene glycol dimethyl ether (4 ml) and water (0.5 ml) water (2 ml) and brine (2ml), and concentrated in vacuo. reverse phase HPLC (30-70% acetonitrile/water) followed by lyophilization yielded the product as an off-white under nitrogen was heated at 65 °C for 16 hours. The triphenylphosphine palladium (0) (0.043 mmol, 50 mg), reaction was concentrated under a nitrogen stream. A solution of the residue in chloroform (2 ml) and trifluoroacetic acid (2 ml) was stirred at ambient A mixture of EX-51 (0.144 mmol, 75 mg), (2temperature for 30 minutes. The reaction was carbonate (0.43 mmol, 140 mg), tetrakis-

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65% ethyl acetate / hexane) yielded 2.88 g (70% yield) of hydrobromic acid (33% in acetic acid, 150 ml) was stirred The combined organic fractions were washed with brine (50 solution, and the pH adjusted to 12 with sodium carbonate (2N). The resulting precipitate was collected by vacuum Purification by silica gel chromatography (50- $\mathbf{EX-5E}$ as an off-white foam. MS (ES, m/z), 638:640 (M+H). with diethyl ether. The residue was dissolved in water (200 ml), neutralized with saturated sodium bicarbonate diluted with diethyl ether to give a tacky precipitate. filtrate was extracted with dichloromethane (3x100 ml). The reaction was The solution was decanted, and the residue was rinsed concentrated in vacuo. The combined residues yielded 5.48 g (95% yield) of EX-5F as a tan solid. MS (ES, filtration, water washed, and dried in vacuo. The ml), dried over magnesium sulfate, filtered, and A solution of EX-5E (14.2 mmol, 9.09 g) in it ambient temperature for 18 hours. 262 m/z), 404:406 (M+H).

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butyldicarbonate (14.3 mmol, 3.55 g), triethylamine (13.5 washed with water (2x100 ml), brine (100 ml), dried over 3.2 g). The reaction was stirred at ambient temperature The residue was crystallized form ethyl acetate / hexane magnesium sulfate, filtered, and concentrated in vacuo. To a stirred suspension of EX-5F (13.5 mmol, 4.47 for 64 hours. The reaction was concentrated in vacuo. nmol, 1.88 ml), and 4-dimethylaminopyridine (1.6 mmol, The residue was diluted with ethyl acetate (300 ml), to yield 3.0 g (44% yield) of EX-5G as an off-white g), in acetonitrile (500 ml) was added di-tertsolid. MS (ES, m/z), 504:506 (M+H).

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added 3-chloroperoxybenzoic acid (64%, 6.3 mmol, 1.71 g). minutes. The reaction was concentrated in vacuo, and the To a stirred solution of EX-5G (5.6 mmol, 2.8 g) in Stirring was continued at ambient temperature for 30 dichloromethane (300 ml) and chloroform (100 ml) was

solid. HRMS calc'd for C₁₁H₂M₂O₃ (M+H): 524.2662. Found: 524.2678. Anal. Calc'd for C₁₁H₂M₂O₃+2.2 TFA, 0.6 H₃O: C, 54.14; H, 4.67; N, 8.91. Found: C, 54.10; H, 4.58; N. 9.07.

Example 6

Using procedures similar to those described in **Example 5** and substituting (2-phenoxyphenyl) boronic acid for (2-benzyloxyphenyl) boronic acid, the product was obtained as an off-white solid. HRWS calc'd for C₁₀H₁₁N₅O₃ (M+H): 510.2505. Found: 510.2508.

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Example 7

7A as a tan solid: ^1H NMR (CDC₁₃) δ 9.06 (t, J = 1.5 Hz, 1 mixture was pump/purged (vacuum/argon) for 3 cycles, and 3.80 g), and potassium acetate (154 mmol , 15.1 g). The to afford 10.7 g (71 % yield) of pure boronate ester EXferrocene]palladium(II) dichloromethane adduct (10 mol*, dark black mixture was recrystallized from acetonitrile (ESI, negative ion mode) (M-H) = 211 (for boronic acid A 250 mL round bottom flask was charged with iodoreaction was stirred at 75 °C overnight. At this time, H), 8.88 (d, J = 1.5 Hz, 2 H), 1.35 (s, 12 H); LC-LRMS the reaction mixture was cooled and concentrated. DMF (200 mL) was added via cannula transfer. The bis(pinacolato)diboron (61.6 mmol, 15.7 g), 3,5-dinitrobenzene (51.4 mmol, 15.1 g), dichloro[1,1'-bis(diphenylphosphino)hydrolysis product).

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A mixture of 3,5-dinitrophenylboronic acid, pinacolester EX-7A (0.85 mmol, 0.25 g) and palladium on carbon (10% dry basis, wet, 0.25 g) in ethanol (75 ml) and water (1 ml) was shaken under hydrogen (40 psi) for 30 minutes. The reaction was filtered and concentrated in vacuo to yield 0.20g (100% yield) of EX-7B as a light gray solid.

MS (ES, m/z), 235 (M+H). ¹HNWR (CDCl³) 8 1.22 (g, 12H), 3.88 (g, 4H), 6.16 (g, 1H), 6.48 (g, 2H).

A mixture of EX-5H (0.29 mmol, 150 mg), EX-7B (0.43 mmol, 101 mg), cesium carbonate (1.16 mmol, 377 mg), tetrakis-triphenylphosphine palladium (0) (0.058 mmol, 67 mg), ethylene glycol dimethyl ether (6 ml) and water (0.75 ml) under nitrogen was heated at 65 °C for 16 hours and at 75 °C for 20 hours. The reaction was concentrated under a nitrogen stream. The residue was eluted through a 5 ml Chemelute tube packed with celite pretreated with 2M sodium carbonate using chloroform and the eluant concentrated under a nitrogen stream. A solution of the residue in chloroform (2 ml) and trifluoroacetic acid (2 ml) was stirred for 30 minutes at ambient temperature followed by concentration under a nitrogen stream.

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Purification by reverse phase HPLC (10-70% acetonitrile/water) followed by lyophilization yielded 60 mg (37% yield) of product as an off-white solid. HDMR (CDCl₃) & 1.26 (d, J = 6.3 Hz, 6H), 3.3-4.5 (br m, 6H), 3.71 (a, 2H), 4.39 (s, 2H), 6.37-6.48 (m, 2H), 6.87 (d, J = 8.7 Hz, 1H), 6.94 (d, J = 8.4 Hz, 1H), 7.12 (d, J = 8.7 Hz, 1H), 7.55 (d, J = 8.1 Hz, 2H), 7.76 (d, J = 8.1 Hz, 2H), 8.81 (t, J = 5.4 Hz, 1H), 9.07 (br s, 1H), 9.27 (br s, 1H). HRMS calc'd for C₂,H₃,0,O₃ (M+H): 448.2461. Pound: 448.2472. Anal. Calc'd for C₃,H₃,0,O₃+2.5 TFA, 1.8 H, 4.58; N, 12.85.

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Example 8

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Using the procedure of Example 7 with 4'-fluoro-2-biphenyl boronic acid, the product was obtained as an off-white solid. HRMS calc'd for C,0H,1N,02F (M+H): 512.2462. Found: 512.2467.

Example 9

Using the procedure of Example 7 with (3-hydroxymethylphenyl)boronic acid, the product was obtained as an off-white solid. HRMS calc'd for C23H30N5O3 (M+H): 448.2349. Found: 448.2349.

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Example 10

Using the procedure of Example 7 with 3-acetylphenylboronic acid, the product was obtained as an off-white solid. HRMS calc'd for $C_8 H_{10} N_9 O_3$ (M+H): 460.2349. Found: 460,2356.

Example 11

Using the procedure of Example 7 with benzothiophene-3-boronic acid, the product was obtained

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as an off-white solid, . HRMS calc'd for $C_{26}H_{28}N_5O_2S$ (M+H): 474.1964. Found: 474.1949.

Example 12

Using the procedure of **Example 7** with transbiphenylethenylboronic acid, the product was obtained as an off-white solid., HRMS calc'd for $C_{26}H_{10}N_5O_2$ (M+H): 444.2400. Found: 444.2396.

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Example 13

Using the procedure of Example 7 with (2-phthalimidomethylphenyl)-boronic acid, the product was obtained as an off-white solid. . HRMS calc'd for C,1H,3N,O, (M+H): 577.2563. Found: 577.2620.

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Following methods disclosed above and using EX-5H as starting material and (3-aminophenyl) boronic acid as a reagent, crude material EX-14A was obtained: (MS (ES, m/z) 533.28 (M+H). EX-14A was used directly in the next step of the procedure. The product was obtained in a yield of 45%. HRMS calc'd for C₂₄H₂₈N₆O₂ (M+H): 433.2352. Found: 433.2368. Anal. Calc'd for C₂₄H₂₈N₆O₂+2.15TFA, 1.05H₂O: C, 48.80; H, 4.67; N, 12.06. Found: C, 48.80; H, 4.57; N, 12.11.

Using the examples and methods described herein previously, the following examples having a amidinoaralkyl or amidinoheteroaralkyl type Y° group could be prepared:

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2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3-aminophenyl]- 6-[N,N-dimethylhydrazino]-1-oxypyridinyl]]acetamide;

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2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3-

aminophenyl] -6-[N-ethyl-N-methylhydrazino]-1-

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oxypyridinyl]]acetamide;
2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3aminophenyl]-5-chloro-6-[N,N-dimethylhydrazino]-1oxypyridinyl]]acetamide;

2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3-aminophenyl]-5-chloro-6-[N-ethyl-N-methylhydrazino]-1-

oxypyridinyl]]acetamide;

2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3,5diaminophenyl]- 6-[N,N-dimethylhydrazino]-1oxypyridinyl]]acetamide;

2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3,5-diaminophenyl]-6-[N-ethyl-N-methylhydrazino]-1-

oxypyridinyl]]acetamide;

2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3,5diaminophenyl]-5-chloro-6-[N,N-dimethylhydrazino]-1oxypyridinyl]]acetamide;

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2-[2-[N-[{4-aminoiminomethylphenyl]methyl]-3-[3,5diaminophenyl]-5-chloro-6-[N-ethyl-N-methylhydrazino]-1oxypyridinyl]]acetamide;

2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3amino-5-carboxyphenyl]- 6-[N,N-dimethylhydrazino]-1oxypyridinyl]]acetamide;

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2-[2-[N-[{4-aminoiminomethylphenyl]methyl]-3-[3amino-5-carboxyphenyl]-6-[N-ethyl-N-methylhydrazino]-1oxypyridinyl]]acetamide;

2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3amino-5-carboxyphenyl]-5-chloro-6-[N,Ndimethylhydrazino]-1-oxypyridinyl]]acetamide; 2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3-

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amino-5-carboxyphenyl]-5-chloro-6-[N-ethyl-Nmethylhydrazino]-1-oxypyridinyl]]acetamide;
2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3amino-5-(N-benzylamidocarbonyl)phenyl]- 6-[N,N-

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amino-5-(N-benzylamidocarbonyl)phenyl] - 6-[N,Ndimethylhydrazino]-1-oxypyridinyl]acetamide;
2-[2-[N-[{4-aminoiminomethylphenyl]methyl}-3-[3-

amino-5-(N-benzylamidocarbonyl)phenyl]-6-[N-ethyl-N-

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methylhydrazino]-1-oxypyridinyl]]acetamide;
2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3-amino-5-(N-benzylamidocarbonyl)phenyl]-5-chloro-6-[N,N-dimethylhydrazino]-1-oxypyridinyl]acetamide;

2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-33-amino-5-(N-benzylamidocarbonyl)phenyl]-5-chloro-6-[N-ethyl-N-

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methylhydrazino]-1-oxypyridinyl]]acetamide.

Using the examples and methods described herein previously, the following further examples having a amidinoaralkyl or amidinoheteroaralkyl type Yo group could be prepared of the formula:

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wherein;

 R^2 is 3-aminophenyl, B is phenyl, A is CH_2 , Y^{α} is 4-amidinobenzyl, and R^1 is chloro,

 R^2 is 3-aminophenyl, B is 3-chlorophenyl, A is CH_2CH_2 Y^{α} is 4-amidinobenzyl, and R^1 is chloro;

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 R^2 is 3-aminophenyl, B is phenyl, A is $CH_2,\ Y^0$ is 4-amidinobenzyl, and R^1 is hydrido;

 R^2 is 3-aminophenyl, B is 2-imidazoyl, A is $CH_2CH_2,\ Y^0$ is 4-amidinobenzyl, and R^1 is chloro,

 R^2 is 3-amidocarbonyl-5-aminophenyl, B is 3-chlorophenyl, A is CH_2CH_2 , Y^o is 4-amidinobenzyl, and R^1 is chloro;

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R² is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is 3-chlorophenyl, A is CH₂CH₂, Y⁰ is 4-amidinobenzyl, and R1

is chloro;

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 R^2 is 3-amino-5-(N-(2-chlorobenzyl) amidocarbonyl) phenyl, B is 3-chlorophenyl, A is CH_3CH_3 , Y^0 is 4-amidinobenzyl, and R^1 is chloro;

R² is 3-amino-5-(N-(2-

chlorobenzyl)amidosulfonyl)phenyl, B is 3-chlorophenyl, A is Ch_Ch_2, Y^0 is 4-amidinobenzyl, and R¹ is chloro;

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R2 is 3-amino-5-(N-(2-

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nophenyl, B is 2-propenyl, A is a bond, Yº

inophenyl, B is ethyl, A is a bond, Y° is

4-amidinobenzyl, and R1 is chloro;

trifluoromethylbenzyl)amidocarbonyl) - phenyl, B is 3-

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chlorophenyl, A is CH2CH2, Y is 4-amidinobenzyl, and R1 is		R ² is 3-aminophenyl, B is ethyl, A is
chloro;		4-amidino-2-fluorobenzyl, and R1 is chloro;
R ² is 3,5-diaminophenyl, B is 3-chlorophenyl, A is		R' is 3-aminophenyl, B is 2-propenyl,
CH,CH,, Y° is 4-amidinobenzyl; and R¹ is chloro;	ហ	is 4-amidinobenzyl, and R' is chloro;
R ² is 3-amino-5-carboxyphenyl, B is 3-chlorophenyl, A		R ² is 3-aminophenyl, B is isopropyl, A
is CH,CH,, Y° is 4-amidinobenzyl, and R¹ is chloro;		is 4-amidino-2-fluorobenzyl, and R1 is chlo
R ² is 3-amidocarbonyl-5-aminophenyl, B is 3-		R ² is 3-aminophenyl, B is isopropyl, A
chlorophenyl, A is CH,CH,, Yo is 4-amidinobenzyl, and R' is		is 4-amidinobenzyl, and R1 is chloro;
hydrido;	10	R ² is 3-aminophenyl, B is 2-butyl, A i
R' is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is		4-amidinobenzyl, and R1 is chloro;
3-chlorophenyl, A is CH2CH3, Y° is 4-amidinobenzyl, and R1		R' is 3-aminophenyl, B is (R)-2-butyl,
is hydrido;		Y° is 4-amidinobenzyl, and R¹ is chloro;
R ² is 3-amino-5-(N-(2-		R ² is 3-aminophenyl, B is 2-propynyl,
chlorobenzyl)amidocarbonyl)phenyl, B is 3-chlorophenyl, A	15	is 4-amidinobenzyl, and R1 is chloro;
is CH ₂ CH ₂ , Y ⁰ is 4-amidinobenzyl, and R ¹ is hydrido;		R ² is 3-aminophenyl, B is 3-pentyl, A
R ² is 3-amino-5-(N-(2-		is 4-amidinobenzyl, and R1 is hydrido;
chlorobenzyl)amidosulfonyl)phenyl, B is 3-chlorophenyl, A		R ² is 3-aminophenyl, B is hydrido, A i
is CH ₂ CH ₂ , Y ⁰ is 4-amidinobenzyl, and R ¹ is hydrido;		amidinobenzyl, and R¹ is chloto;
R ² is 3-amino-5-(N-(2-	20	R' is 3-aminophenyl, B is ethyl, A is
trifluoromethylbenzyl)amidocarbonyl) - phenyl, B 18 3-		amidinobenzyl, and R¹ is chloro;
chlorophenyl, A is CH2CH, Y° is 4-amidinobenzyl, and R¹ is		R ² is 3-aminophenyl, B is 2-methypropy
hydrido;		Y° is 4-amidinobenzyl, and R¹ is chloro;
R' is 3,5-diaminophenyl, B is 3-chlorophenyl, A is		R' is 3-aminophenyl, B is 2-propyl, A
CH ₂ CH ₂ , Y° is 4-amidinobenzyl, and R1 is hydrido;	25	4-amidinobenzyl, and R, is chloro;
R ² is 3-amino-5-carboxyphenyl, B is 3-chlorophenyl, A		R ² is 3-aminophenyl, B is propyl, A 16
is CH,CH,, Y° is 4-amidinobenzyl, and R¹ is hydrido;		4-amidino-2-fluorobenzyl, and R is chloro

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 R^2 is 3-aminophenyl, B is tert-butyl, A is a bond, Y^{o} R^2 is 3-aminophenyl, B is tert-butyl, A is a bond, Y° inophenyl, B is 2-butyl, A is a bond, Y^0 is inophenyl, B is 2-propynyl, A is a bond, Y° dnophenyl, B is 2-methypropyl, A is a bond, ninophenyl, B is 2-propyl, A is CH,CH, Y° is R' is 3-aminophenyl, B is 6-amidocarbonylhexyl, A is inophenyl, B is hydrido, A is CH2, Y° is 4ninophenyl, B is propyl, A is a bond, Yº is inophenyl, B is isopropyl, A is a bond, Y° inophenyl, B is isopropyl, A is a bond, Y° inophenyl, B is (R)-2-butyl, A is a bond, R² is 3-aminophenyl, B is 2-methylpropyl, A is a inophenyl, B is 3-pentyl, A is a bond, Inophenyl, B is ethyl, A is CH2, Y° is R' is 3-aminophenyl, B is 3-hydroxypropyl, A is a bond, Yo is 4-amidinobenzyl, and R1 is chloro; bond, Y° is 4-amidinobenzyl, and R¹ is chloro; fluorobenzyl, and R1 is chloro; 4-amidino-2-fluorobenzyl, and R¹ is chloro; benzyl, and R1 is chloro; benzyl, and R¹ is chloro; is 4-amidinobenzyl, and R' is hydrido; nzyl, and R1 is hydrido; is 4-amidinobenzyl, and R¹ is chloro; zyl, and R1 is chloro; zyl, and R1 is chloro; 1, and R, is chloro; , and R1 is chloro; and R' is chloro; and R1 is chloro; 35 30

R2 is 2-methyl-3-aminophenyl, B is isopropyl, A is a

bond, Yo is 4-amidinobenzyl, and R1 is chloro;

 R^2 is 3-aminophenyl, B is ethyl, A is a bond, Y^0 is

bond, Yo is 4-amidinobenzyl, and R1 is chloro;

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R² is 5-amino-2-fluorophenyl, B is isopropyl, A is a

R² is 3-aminophenyl, B is (S)-2-butyl, A is a bond,

Y° is 4-amidinobenzyl, and R¹ is chloro;

Y° is 4-amidinobenzyl, and R¹ is chloro;

a bond,

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R² is 3-aminophenyl, B is 2,2,2-trifluoroethyl, A is

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 \mathbb{R}^2 is 3-aminopheny1, B is buty1, A is a bond, \mathbb{Y}^0 is bond, Yo is 4-amidino-2-fluorobenzyl, and R1 is chloro; 4-amidinobenzyl, and R1 is chloro; R² is 3-aminophenyl, B is 1-methoxy-2-propyl, A is R2 is 3-aminophenyl, B is 2-methoxyethyl, A is a bond, Yo is 4-amidinobenzyl, and R1 is chloro; bond, Y° is 4-amidinobenzyl, and R¹ is chloro,

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 R^2 is 3-aminophenyl, B is 2-propyl, A is a bond, Y^{o} is 5-amidino-2-thienylmethyl, and R1 is chloro; R2 is 5-amino-2-methylthiophenyl, B is 2-propyl, A is a bond, Y^0 is 4-amidinobenzyl, and \mathbb{R}^1 is chloro,

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R2 is 3-amino-5-carboxyphenyl, B is isopropyl, A is a R² is 3-amino-5-carbomethoxyphenyl, B is isopropyl, A bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

 R^2 is 3-aminophenyl, B is isopropyl, A is a bond, Y^{o} is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

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R² is 3-amino-5-carboxamidophenyl, B is isopropyl, A is 4-amidinobenzyl, and R1 is bromo;

is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro; R2 is 3-amino-5-(N-benzyl-N-

methylamidocarbonyl)phenyl, B is isopropyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro; R2 is 3-amino-5-(N-(1-

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bond, Y° is 4-amidinobenzyl, and R¹ is chloro; R' is 3-amino-5-(N-(2-pheny1-2-25

phenylethyl) amidocarbonyl) phenyl, B is isopropyl, A is a

propyl)amidocarbonyl)phenyl, B is isopropyl, A is a bond Y° is 4-amidinobenzyl, and R¹ is chloro;

dichlorobenzyl)amidocarbonyl)phenyl, B is isopropyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro; R² is 3-amino-5-(N-(2,4-R2 is 3-amino-5-(N-(4-30

bromobenzyl) amidocarbonyl) phenyl, B is isopropyl, A is a bond, Yº 18 4-amidinobenzyl, and R' is chloro;

R² is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is isopropyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is

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R2 is 3-amino-5-(N-(2-

chloro;

chlorobenzyl)amidocarbonyl)phenyl, B is isopropyl, A is bond, Y° is 4-amidinobenzyl, and R¹ is chloro; R2 1s 3-amino-5-(N-(2-

trifluoromethylbenzyl) amidocarbonyl) phenyl, B is

isopropyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro;

R2 is 3-amino-5-(N-(3-

fluorobenzyl) amidocarbonyl) phenyl, B is isopropyl, A is bond, Y° is 4-amidinobenzyl, and R¹ is chloro, 10

R2 is 3-amino-5-(N-(3-

isopropyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is trifluoromethylbenzyl) amidocarbonyl) phenyl, B 1s chloro;

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R2 is 3-amino-5-(N-isobutylamidocarbonyl)phenyl, B is isopropyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro; R² is 3-amino-5-(N-cyclobutylamidocarbonyl)phenyl, B is isopropyl, A is a bond, Y^0 is 4-amidinobenzyl, and \mathbb{R}^1

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R2 is 3-amino-5-(N-cyclopentylamidocarbonyl)phenyl, is isopropyl, A is a bond, Y^0 is 4-amidinobenzyl; and R^1 is chloro; is chloro;

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Ø R² is 3-amino-5-(N-cycloheptylamidocarbonyl)phenyl, is isopropyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro;

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R2 18 3-amino-5-(N-(2-

pyridylmethyl)amidocarbonyl)phenyl, B is isopropyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro; pyridylmethyl)amidocarbonyl)phenyl, B is isopropyl, A is

R2 18 3-amino-5-(N-(3-

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a bond, Yº is 4-amidinobenzyl, and R¹ is chloro;

methoxyphenyl)ethyl)amidocarbonyl)phenyl, B is isopropyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro; R2 is 3-amino-5-(N-(2-(4-35

phenylpropyl)amidocarbonyl)phenyl, B is isopropyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro; R² is 3-amino-5-(N-(2,2-R is 3-amino-5-(N-(3-

diphenylethyl)amidocarbonyl)phenyl, B is isopropyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro; R² is 3-amino-5-(N-(2-

naphthylmethyl)amidocarbonyl)phenyl, B is isopropyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

ylmethyl) amidocarbonyl) phenyl, B is isopropyl, A is a R' is 3-amino-5-(N-(1,2,3,4-tetrahydronaphth-2bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro;

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 R^2 is 3-aminophenyl, B is 2-propyl, A is a bond, Y^{o}

 R^2 is 3-carboxyphenyl, B is 2-propyl, A is a bond, $Y^{\rm o}$ is 4-amidino-3-fluorobenzyl, and R¹ is hydrido;

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R' is 3-aminophenyl, B is 2-propyl, A is a bond, Y^o is 4-amidino-3-fluorobenzyl, and R1 is chloro; is 4-amidinobenzyl, and R¹ is hydrido;

R' is 3,5-diaminophenyl, B is 2,2,2-trifluoroethyl, A is a bond, Y° is 4-amidinobenzyl, and R^{1} is chloro;

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R' is 3,5-diaminophenyl, B is (S)-2-butyl, A is a Y° is 4-amidinobenzyl, and R¹ is chloro;

R' is 3,5-diaminophenyl, B is isopropyl, A is a bond, R' is 3,5-diaminophenyl, B is isopropyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

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 R^2 is 3,5-diaminophenyl, B is ethyl, A is a bond, Y^0 Y^{0} is 4-amidino-2-fluorobenzylbenzyl, and R^{1} is chloro; is 4-amidinobenzyl, and R1 is chloro;

 R^2 is 3,5-diaminophenyl, B is ethyl, A is a bond, Y° R² is 3-amino-5-carboxyphenyl, B is 2,2,2is 4-amidino-2-fluorobenzyl, and R1 is chloro;

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R² is 3-amino-5-carboxyphenyl, B is (S)-2-butyl, A is trifluoroethyl, A is a bond, Y^0 is 4-amidinobenzyl, and \mathbb{R}^1

is 3amino-5-carboxyphenyl, B is isopropyl, A is a

a bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

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18 bond, Y^0 is 4-amidino-2-fluorobenzylbenzyl, and R^1

chloro;

R2 is 3-amino-5-carboxyphenyl, B is ethyl, A is a bond, Yo is 4-amidinobenzyl, and R1 is chloro; R2 is 3-amino-5-carboxyphenyl, B is ethyl, A is a

2,2,2-trifluoroethyl, A is a bond, Y° is 4-amidinobenzyl, R' 18 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is bond, Yo is 4-amidino-2-fluorobenzyl, and R' is chloro; and R' is chloro;

(S)-2-butyl, A is a bond, Yo is 4-amidinobenzyl, and R1 is R2 is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is chloro;

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R' is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is isopropyl, A is a bond, Y^0 is 4-amidino-2-

fluorobenzylbenzyl, and R1 is chloro;

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R2 is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is ethyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro;

ethyl, A is a bond, Y^{α} is 4-amidino-2-fluorobenzyl, and R^{1} R' is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is is chloro;

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R' is 3,5-diaminophenyl, B is isopropyl, A is a bond, Yº is 4-amidinobenzylbenzyl, and R¹ is hydrido;

R2 is 3-aminophenyl, B is cyclopropyl, A is a bond, Yo is 4-amidinobenzyl, and R1 is chloro;

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 R^2 is 3-aminophenyl, B is cyclobutyl, A is a bond, Y^α R^2 is 3-aminophenyl, B is cyclobutyl, A is a bond, Y^{o} is 4-amidino-2-fluorobenzyl, and R1 is chloro;

R' is 3-aminophenyl, B is cyclopropyl, A is a bond, Y° is 4-amidino-2-fluorobenzyl, and R¹ is chloro; is 4-amidinobenzyl, and R1 is chloro;

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 R^2 is 3-aminophenyl, B is cyclobutyl, A is a bond, Y^{o} is 4-amidinobenzyl, and R¹ is hydrido;

R² is 3-aminophenyl, B is cyclobutyl, A is a bond, Y^o R' is 3-aminophenyl, B is cyclopentyl, A is a bond, is 4-amidino-3-fluorobenzyl, and R1 is chloro;

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- R^2 is 3-aminophenyl, B is cyclopropyl, A is CH, Y^0 is R' is 5-amino-2-thienyl, B is cyclobutyl, A is a bond, Y^{0} is 4-amidinobenzyl, and R^{1} is chloro; Y° is 4-amidinobenzyl, and R¹ is chloro;

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R2 is 3-aminophenyl, B is 2-(2R)-bicyclo[2.2.1]heptyl, A is a bond, Yo is 4-amidinobenzyl, and Ri is 4-amidinobenzyl, and R1 is chloro;

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R' is 3-aminophenyl, B is cyclopentyl, A is a bond, chloro;

Y° is 4-amidino-2-fluorobenzyl, and R¹ is chloro;

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 R^2 is 3-aminophenyl, B is cyclohexyl, A is $CH_2CH_2, \ Y^{\alpha}$ is 4-amidinobenzyl, and R¹ is hydrido;

 R^2 is 3-aminophenyl, B is oxalan-2-yl, A is $CH_7,\ Y^0$ is

R² is 3-aminophenyl, B is 1-piperidinyl, A is CH₂CH₂, 4-amidinobenzyl, and R¹ is chloro;

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R' is 3-aminophenyl, B is 1-pyrrolidinyl, A is CH, CH,, Y° is 4-amidinobenzyl, and R¹ is chloro;

R' is 3-amino-5-carbomethoxyphenyl, B is cyclobutyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is hydrido; γ^{o} is 4-amidinobenzyl, and R^{1} is chloro; 20

R² is 3-amino-5-carboxyphenyl, B is cyclobutyl, A is is 3,5-diaminophenyl, B is cyclobutyl, A is a a bond, Y° is 4-amidinobenzyl, and R¹ is hydrido; bond, Y° is 4-amidinobenzyl, and R¹ is hydrido;

R' is 2-amino-6-carboxy-4-pyridyl, B is cyclobutyl, A R² is 3-amino-5-carbomethoxyphenyl, B is cyclobutyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro, is a bond, Yo is 4-amidinobenzyl, and R¹ is hydrido;

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R' 1s 3-amino-5-carboxyphenyl, B is cyclobutyl, A is R2 is 3,5-diaminophenyl, B is cyclopropyl, A is a a bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

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bond, Y° is 4-amidino-2-fluorobenzyl, and R¹ is chloro; R' is 3,5-diaminophenyl, B is cyclobutyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

bond, Y° is 4-amidino-2-fluorobenzyl, and R¹ is chloro; R' is 3,5-diaminophenyl, B is cyclopropyl, A is a 35

Ø R' is 3,5-diaminophenyl, B is cyclobutyl, A is bond, Y^0 is 4-amidinobenzyl, and R^1 is hydrido;

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R2 is 3,5-diaminophenyl, B is cyclobutyl, A is a

bond, Y is 4-amidino-3-fluorobenzyl, and R is chloro; R' is 3,5-diaminophenyl, B is cyclopentyl, A is a

R2 is 3-carboxy-5-aminophenyl, B is cyclopropyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro; bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

R' is 3-carboxy-5-aminophenyl, B is cyclobutyl, A is

R' is 3-carboxy-5-aminophenyl, B is cyclopropyl, A is a bond, Y° is 4-amidino-2-fluorobenzyl, and R¹ is chloro; a bond, Y° is 4-amidino-2-fluorobenzyl, and R¹ is chloro;

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R' is 3-carboxy-5-aminophenyl, B is cyclobutyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is hydrido;

R' is 3-carboxy-5-aminophenyl, B is cyclopentyl, A is R' is 3-carboxy-5-aminophenyl, B is cyclobutyl, A is a bond, Yo is 4-amidino-3-fluorobenzyl, and R' is chloro;

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R' is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is a bond, Yo is 4-amidinobenzyl, and R1 is chloro;

cyclopropyl, A is a bond, Y° is 4-amidinobenzyl, and R^{1} is chloro;

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R' is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is cyclobutyl, A is a bond, Y^0 is 4-amidino-2-fluorobenzyl, and R' is chloro;

R¹ is R' is 3-amino-5- (N-benzylamidocarbonyl) phenyl, B is cyclobutyl, A is a bond, Yo is 4-amidinobenzyl, and chloro;

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cyclopropyl, A is a bond, Y° is 4-amidino-2-fluorobenzyl, R2 is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is R² is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is and R1 is chloro;

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R1 18 R2 is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is cyclobutyl, A is a bond, Yo is 4-amidinobenzyl, and hydrido;

cyclobutyl, A is a bond, Y° is 4-amidino-3-fluorobenzyl, and R' is chloro;

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R² is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is cyclopentyl, A is a bond, Y° is 4-amidinobenzyl, and R² is chloro;

R2 is 3-amino-5-(N-(2-

chlorobenzyl)amidosulfonyl)phenyl, B is cyclopropyl, A is a bond, Y° is 4-amidinobenzyl, and \mathbb{R}^1 is chloro;

R² is 3-amino-5-(N-(2-

chlorobenzyl)amidosulfonyl)phenyl, B is cyclobutyl, A is a bond, Y^o is 4-amidino-2-fluorobenzyl, and R^1 is chloro, R^2 is 3-amino-5- $(N-\{2-$

chlorobenzyl)amidosulfonyl)phenyl, B is cyclobutyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro;

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R2 is 3-amino-5-(N-(2-

chlorobenzyl)amídosulfonyl)phenyl, B is cyclopropyl, A is a bond, Y° is 4-amidino-2-fluorobenzyl, and R¹ is chloro, R² is 3-amino-5-(N-(2-

chlorobenzyl) amidosulfonyl) phenyl, B is cyclobutyl, A is a bond, Y° is 4-amidinobenzyl, and R^1 is hydrido;

R2 is 3-amino-5-(N-(2-

20 chlorobenzyl)amidosulfonyl)phenyl, B is cyclobutyl, A is a bond, Y° is 4-amidino-3-fluorobenzyl, and R¹ is chloro;

 R^2 is 3-amino-5-(N-(2-chlorobenzyl) amidosulfonyl) phenyl, B is cyclopentyl, A is a bond, $Y^{\rm o}$ is 4-amidinobenzyl, and $R^{\rm i}$ is chloro;

R² is 3-amino-5-(N-(2-

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trifluoromethylbenzyl)amidocarbonyl)-phenyl, B is cyclopropyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is

R² is 3-amino-5-(N-(2-

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trifluoromethylbenzyl) amidocarbonyl) -phenyl, B is
cyclobutyl, A is a bond, Y° is 4-amidino-2-fluorobenzyl,
and R¹ is chloro;

R² is 3-amino-5-(N-(2-

trifluoromethylbenzyl>amidocarbonyl>-phenyl, B is
cyclobutyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is
chloro;

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R2 is 3-amino-5-(N-(2-

trifluoromethylbenzyl) amidocarbonyl)-phenyl, B is cyclopropyl, A is a bond, Y^o is 4-amidino-2-fluorobenzyl and R¹ is chloro;

R² is 3-amino-5-(N-(2-

trifluoromethylbenzyl) amidocarbonyl) -phenyl, B is cyclobutyl, A is a bond, Y^o is 4-amidinobenzyl, and R^1 is hydrido;

R² is 3-amino-5-(N-(2-

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trifluoromethylbenzyl)amidocarbonyl)-phenyl, B is cyclobutyl, A is a bond, Y° is 4-amidino-3-fluorobenzyl, and R^1 is chloro;

R2 is 3-amino-5-(N-(2-

trifluoromethylbenzyl)amidocarbonyl)-phenyl, B 1s
cyclopentyl, A 1s a bond, Y° is 4-amidinobenzyl, and R¹ is
chloro.

Using the examples and methods described herein previously, the following further additional examples having a guanidinoalkyl type Y^{AT} group could be prepared of the formula:

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wherein;

 R^2 is 3-aminophenyl, B is phenyl, A is $CH_2CH_2,\ Y^{4T}$ is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R^1 is aminomethyl, and X° is chloro;

R² is 3,5-diaminophenyl, B is phenyl, A is CH₂CH₂, Y^M is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R¹ is aminomethyl, and X° is chloro;

CH₂CH₂, Y^{AT} is 5-guanidino-1-oxo-1-(2-thiazoly1)-2-pentyl, R2 is 3-carboxy-5-aminophenyl, B is phenyl, A is R' is aminomethyl, and X° is chloro;

thiazoly1)-2-pentyl, R' is aminomethyl, and X° is chloro; R2 is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is phenyl, A is CH2CH2, YM is 5-guanidino-1-oxo-1-(2-

'n

bond, YAT is 5-guanidino-1-oxo-1-(2-thiazoly1)-2-pentyl, R1 R' is 3,5-diaminophenyl, B is isopropyl, A is single is aminomethyl, and X° is chloro;

R2 is 3-carboxy-5-aminophenyl, B is isopropyl, A is single bond, YAT is 5-guanidino-1-oxo-1-(2-thiazolyl)-2pentyl, R1 is aminomethyl, and X° is chloro;

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R2 is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is isopropyl, A is single bond, YAT is 5-guanidino-1-oxo-1-(2-thiazoly1) -2-pentyl, R¹ is aminomethyl, and X° is chloro;

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bond, Y^{AT} is S-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R¹ R2 is 3,5-diaminophenyl, B is cyclobutyl, A is single is aminomethyl, and X° is chloro;

R2 is 3-carboxy-5-aminophenyl, B is cyclobutyl, A is single bond, Y^{AT} is 5-guanidino-1-oxo-1-(2-thiazolyl)-2pentyl, R1 is aminomethyl, and X° is chloro;

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cyclobutyl, A is single bond, YAT is 5-guanidino-1-oxo-1-R2 is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is (2-thiazoly1) -2-pentyl, R^1 is aminomethyl, and X° is chloro;

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 R^2 is 3-aminophenyl, B is phenyl, A is $CH_2CH_2,\ Y^{AT}$ is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R1 is chloro, and X° is hydrido;

 R^2 is 3,5-diaminophenyl, B is phenyl, A is $CH_3CH_2,\ Y^{AT}$ CH,CH,, YAT is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R2 18 3-carboxy-5-aminophenyl, B is phenyl, A is is 5-guanidino-1-oxo-1-(2-thiazoly1)-2-penty1, R' is chloro, and X° is hydrido;

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R' is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is R1 is chloro, and Xº is hydrido;

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thiazolyl)-2-pentyl, R¹ is chloro, and X° is hydrido; phenyl, A is CH,CH2, YAT is 5-guanidino-1-oxo-1-(2-

bond, YM is 5-guanidino-1-oxo-1-(2-thiazoly1)-2-pentyl, R1 R² is 3,5-diaminophenyl, B is isopropyl, A is single is chloro, and X° is hydrido;

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R2 is 3-carboxy-5-aminophenyl, B is isopropyl, A is single bond, YM is 5-guanidino-1-oxo-1-(2-thiazolyl)-2pentyl, R' is chloro, and X° is hydrido; R' is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is isopropyl, A is single bond, YAT is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R' is chloro, and X° is hydrido;

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bond, Y** is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R1 R² is 3,5-diaminophenyl, B is cyclobutyl, A is single is chloro, and X° is hydrido;

R2 is 3-carboxy-5-aminophenyl, B is cyclobutyl, A is single bond, YM is 5-guanidino-1-oxo-1-(2-thiazolyl)-2pentyl, R1 is chloro, and Xº is hydrido;

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cyclobutyl, A is single bond, YM is 5-guanidino-1-oxo-1-R' is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is (2-thiazolyl)-2-pentyl, R1 is chloro, and X° is hydrido.

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esters of carboxylic, sulfonic, carbamic, phosphonic, and Alternatively, derivatized Formula (I or A) compounds can form of an alcohol or phenol can be readily converted to possessing hydroxyl, thiol, and amine functional groups phosphoric acids. Acylation to form a carboxylic acid comounds of Formula (I or A). A hydroxyl group in the anhydrides and acid chlorides can also be used. Such chloride. The corresponding aryl and heteroaryl acid further transforming the derivatized intermediate to ester is readily effected using a suitable acylating Intermediates in the processes of preparation before reagent such as an aliphatic acid anhydride or acid reactions are generally carried out using an amine Formula (I or A) compounds of this invention can be converted to a wide variety derivatives. be obtained by first derivatizing one or more

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corresponding primary or secondary amine. A primary amine aralkyl, heteroaralkyl, alkoxyalkyl, aralkyloxyalkyl, and thiol group present can be converted to the corresponding respectively, of an acid scavenger are used concurrently. be obtained by first alkylating one or more intermediates such as DMF, DMSO, THF, and similar, comparable solvents thioether derivatives analogous to those of alcohols and phenols using the same reagents and comparable reaction present can be converted to the corresponding secondary, conditions. Compounds of Formula (I or A) that have at can also be used. Such reactions are generally carried amide, and n-butyl lithium using an inert polar solvent Alkylation to form an ether is readily effected using a heteroaralkyloxyalkyl bromides, iodides, and sulfonates tertiary or quaternary ammonium derivative. Quaternary appropriate bromides, iodides, and sulfonates analogous Alternatively, alkylated Formula (I or A) compounds can alkylating reagent with a stoichiometric amount of the amine (i.e., one equivalent with a tertiary amine, two transforming the alkylated intermediate to comounds of primary and secondary amines, two and one equivalents, Secondary or tertiary amines can be prepared from the hydride, potassium t-butoxide, sodium amide, lithium Compounds of Formula (I or A) that have at least one least one primary, secondary or tertiary amine group to those used with alcohols and phenols. Conditions involve reaction of the amine by warming it with the suitable alkylating reagent such as an alkyl bromide, out using an alkoxide forming reagent such as sodium Formula (I or A). A hydroxyl group of compounds of Formula (I or A) can be readily converted to ethers. amine catalyst such as pyridine in an inert solvent. alkyl iodide or alkyl sulfonate. The corresponding with a secondary, and three with a primary). With ammonium derivatives can be prepared using the in the processes of preparation before further

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group present can be converted to the corresponding amide

derivatives. Amides of carboxylic acids can be prepared

using the appropriate acid chloride or anhydrides with

those of alcohols and phenols using the same reagents and

comparable reaction conditions. Compounds of Formula (I

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or A) that have at least one primary or secondary amine

have at least one thiol group present can be converted to

the corresponding thioesters derivatives analogous to

can be prepared using the corresponding acid chloride and

similar reagents. Compounds of Formula (I or A) that

catalyst such as pyridine in an inert solvent. Similarly,

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reacting a hydroxyl group with isocyanates and carbamoyl chlorides. Sulfonate, phosphonate, and phosphate esters

carbamic acid esters (urethanes) can be obtained by

reaction conditions analogous to those used with alcohols

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and phenols. Ureas of the corresponding primary or

secondary amine can be prepared using isocyanates

directly and carbamoyl chlorides in the presence of an

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Youse's Modern Synthetic Reactions, W. A. Benjamin, Inc.,

methods for preparing these derivatives can be found in

hydroxide or a tertiary amine. Suitable procedures and

sulfonyl chloride in the presence of aqueous sodium

Sulfonamides can be prepared from the corresponding

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acid scavenger such as triethylamine or pyridine.

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possessing hydroxyl, thiol, and amine functional groups Formula (I or A) compounds of this invention

can be alkylated to a wide variety of derivatives.

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hydroxyl, thiol, and amines of compounds of Formula (I or

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references cited above, which are incorporated herein by

A) are available from commercial sources or the

Organic Synthesis, Volume 1, John Wiley & Sons. Reagents

of a wide variety that can be used to derivatize

Identification of Organic Compounds, 5th Edition, John

Shriner, Fuson, and Curtin in The Systematic

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Wiley & Sons, and Fieser and Fieser in Reagents for

Formula (I or A) are available from commercial sources or the references cited above, which are incorporated herein by DesMarteau in J. Chem. Soc. Chem. Commun. 2241 (1998). House's Modern Synthetic Reactions, W. A. Benjamin, Inc., monoalkylated amine. Additional suitable procedures and methods for preparing these derivatives can be found in cyanoborohydride in the presence of glacial acetic acid. 1,1,3,3-tetramethylguanidine), gives the monomethylated protected amine. Removal of the protecting group using Perfluoroalkyl derivatives can be prepared as described nucleophilic base, such as Barton's base (2-tert-butylderivatize hydroxyl, thiol, and amines of compounds of Identification of Organic Compounds, 5th Edition, John group, such as trifluoroacetyl. An alkylating agent, protecting the amine with a ready cleaved protecting Wiley & Sons, and Fieser and Fieser in Reagents for A primary amine can be monoalkylated by first monocan be dialkylated by reductive amination using an such as dimethylsulfate, in the presence of a non-Organic Synthesis published by John Wiley & Sons. iqueous potassium hydroxide gives the desired Shriner, Fuson, and Curtin in The Systematic Reagents of a wide variety that can be used aldehyde, such as formaldehyde, and sodium by reference.

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Assays for Biological Activity

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TF-VIIa Assay

In this assay 100 nM recombinant soluble tissue factor and 2nM recombinant human factor VIIa are added to a 96-well assay plate containing 0.4 mM of the substrate, N-Methylsulfonyl-D-phe-gly-arg-p-nitroaniline and either inhibitor or buffer (5 mM CaCl₂,50 mM Tris-HCl, pH 8.0, 100 mM NaCl, 0.1% BSA). The reaction, in a final volume

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of 100 ul is measured immediately at 405 nm to determine background absorbance. The plate is incubated at room temperature for 60 min, at which time the rate of hydrolysis of the substrate is measured by monitoring the reaction at 405 nm for the release of p-nitroaniline. Percent inhibition of TF-VIIa activity is calculated from OD405nm value from the experimental and control sample.

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а Аввау

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Human factor Xa (0.3 nM) and 0.15 mM N-a-Benzyloxycarbonyl-D-arginyl-L-glycyl-L-arginine-p-nitroaniline-dihydrochloride (S-2765) are added to a 96-well assay plate containing either inhibitor or buffer (50 mM Tris-HCl, pH 8.0, 100 mM Nacl, 0.1% BSA). The reaction, in a final volume of 100 ul is measured immediately at 405 nm to determine background absorbance. The plate is incubated at room temperature for 60 min, at which time the rate of hydrolysis of the substrate is measured by monitoring the reaction at 405 nm for the release of p-nitroaniline. Percent inhibition of Xa activity is calculated from OD₄₀₅nm value from the experimental and control sample.

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Thrombin Assay

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Human thrombin (0.28 nM) and 0.06 mM H-D-Phenylalanyl-L-pipecolyl-L-arginine-p-nitroaniline dihydrochloride are added to a 96-well assay plate containing either inhibitor or buffer (50 mM Tris-HCl, pH 8.0, 100 mM NaCl, 0.1% BSA). The reaction, in a final volume of 100 ul is measured immediately at 405 nm to determine background absorbance. The plate is incubated at room temperature for 60 min, at which time the rate of hydrolysis of the substrate is measured by monitoring the reaction at 405 nm for the release of p-nitroaniline. Percent inhibition of thrombin activity is calculated from OD₄₀₃nm value from the experimental and control

sample.

Trypsin Assay

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Trypsin (5 ug/ml; type IX from porcine pancreas) and 0.375 mM N-α-Benzoyl-L-arginine-p-nitroanilide (L-BAPNA) are added to a 96-well assay plate containing either inhibitor or buffer (50 mM Tris-HCl, pH 8.0, 100 mM NaCl, 0.1% BSA). The reactions, in a final volume of 100 ul are measured immediately at 405 nm to determine background absorbance. The plate is incubated at room temperature for 60 min, at which time the rate of hydrolysis of the substrate is measured by monitoring the reaction at 405 nm for the release of p-nitroaniline. Percent inhibition of trypsin activity is calculated from OD405nm value from the experimental and control sample.

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Recombinant soluble TF, consisting of amino acids 1-219 of the mature protein sequence was expressed in E. coli and purified using a Mono Q Sepharose FPLC.
Recombinant human VIIa was purchased from American Diagnostica Greenwich CT and chromogenic substrate N-Methylaulfonyl-D-phe-gly-arg-p-nitroaniline was prepared by American Peptide Company, Inc., Sunnyvale, CA. Factor Xa was obtained from Enzyme Research Laboratories, South Bend IN, thrombin from Calbiochem, La Jolla, CA, and trypsin and L-BAPNA from Sigma, St. Louis MO. The chromogenic substrates S-2765 and S-2238 were purchased from Chromogenix, Sweden.

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Using bioassay procedures described herein, the biological activity of the compounds of Example 1 through Example 14 are summarized in Table 1.

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Table 1. Inhibitory Activity of Substituted Pyridines toward Factor Xa, TF-VIIA, Thrombin II, and Trypsin II.

Example	TF-VIIA	Factor Xa	Thrombin	Trpysin
Number	ICso	IC, (uM)	H	Ħ
	(Mn)		ICso (uM)	IC ₅₀ (uM)
H	2.46	27% @ 30	0.71	90.0
		Mn		
2	0.07	268 @ 30	7.13	0.02
		Mn		
3	0.72	>100	>100	0.158
4	0.241	>100	8.8	0.02
ស	2.38	>100	0.37	0.1
9	6.94	>100	86.5	0.17
_	0.084	>100	60.7	0.022
8	18	75	48.6	0.47
6	1.72	>100	9.9	0.21
10	1.7	40%@100uM	3	0.035
11	5.6	21	39.5	0.079
12	23% at	>100	29	66.0
	100uM			
13	1.42	>100	12.03	0.121
14	0.155	>100	9.6	<0.14

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What we claim is:

CLAIMS:

A compound having the structure:

wherein

 $X_1,\ X_2,\ X_3\ X_4,\ X_5,$ and X_6 are each ring atoms defining a 6 membered heterocyclic or aromatic ring;

 $X_{\lambda},\ X_{\lambda},$ and X_{ε} are independently carbon or nitrogen;

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X, is carbon;

or sulfur, provided at least one of $X_1,\ X_4,$ and X_6 is other X_s and X_s are independently carbon, nitrogen, oxygen than carbon when X2 is carbon;

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covalently bonded to X1, Z3 is covalently bonded to X3, and Z,, respectively, are covalently bonded to different ring independently being a covalent bond or comprising one or $L_1,\ L_3$ and L_4 are linkages through which $Z_1,\ Z_3,\ and$ atoms of the 6 membered heterocyclic or aromatic ring more atoms through which $Z_1,\ Z_3,$ and Z_4 are covalently $Z_{\bf k}$ is covalently bonded to $X_{\bf k}$, each of $L_{\bf k}$, $L_{\bf k}$ and $L_{\bf k}$ defined by X1, X2, X1, X4, X5, and X6, wherein Z1 is bonded to X1, X3 and X4, respectively;

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amidine, guanidine, amino, or aminoalkyl group, the ring membered substituted heterocyclic or aromatic ring, the substituents of the hydrocarbyl or ring comprising an Z_3 is a substituted hydrocarbyl, or a 5 or 6

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substituted at any position with halogen, hydroxy, or atoms of the 5 or 6 membered heterocyclic or aromatic ring of Z, being carbon, sulfur, nitrogen, or oxygen, wherein the 5 or 6 membered ring is optionally alkyl; Z4 comprises hydrocarbyl, substituted hydrocarbyl or a 5 or 6-membered heterocyclic ring, the ring atoms of the 5 or 6-membered heterocyclic ring being carbon, sulfur, nitrogen or oxygen;

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 $\mathbf{Z_1}$ is hydrogen, hydrocarbyl, or substituted hydrocarbyl; and

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2, is a hydrogen bond acceptor covalently or datively bonded to X2.

The compound of claim 1 wherein

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aromatic ring substituted with an amidine group, the ring atoms of the 5 or 6 membered heterocyclic or aromatic substituted at any position with halogen, hydroxy, or ring of Z, being carbon, sulfur, nitrogen, or oxygen, Z, comprises a 5 or 6 membered heterocyclic or wherein the 5 or 6 membered ring is optionally alkyl;

carboxylic ring, the ring atoms of the 5 or 6 membered Z, comprises a 5 or 6 membered heterocyclic or heterocyclic or carboxylic ring of Z, being carbon, nitrogen, oxygen, or sulfur; and

Z_i is hydrocarbyl or substituted hydrocarbyl.

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membered heterocyclic or carbocyclic ring comprising \mathbf{Z}_{\bullet} is ring atoms each of which is in the beta position relative bonded to one of said beta positions and the other of Ra substituted with two substituents, R42 and R44, and two and R4 is covalently bonded to the other of said beta to the ring atom of Z4 through which Z4 is covalently linked to X,, wherein one of R,, and R,, is covalently The compound of claim 2 wherein the 5 or 6

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positions.

4. The compound of claim 3 wherein R₄₂ is amino and R₄₄ is hydrogen, hydrocarbyl, substituted hydrocarbyl, heterocyclo, halogen, or a substituted or unsubstituted heteroatom selected from nitrogen, oxygen, sulfur and phosphorous.

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5. The compound of claim 2 wherein the 5 or 6 membered heterocyclic or aromatic ring comprising Z, is optionally substituted at any position with fluorine, methyl or hydroxy.

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6. The compound of each of claims 1, 2 or 3 wherein the 5 or 6 membered heterocyclic or aromatic ring comprising 2, is substituted with a derivatived amidine which, upon hydrolysis, oxidation, reduction or elimination yields an amidine group.

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- 7. The compound of claim 1 or 2 wherein L, is selected from the group consisting of a glycine derivative, an alanine derivative, an amino derivative, or a sulfonyl derivative.
- 8. The compound of claim 1 or 2 wherein L_i is covalently bonded directly to X_ϵ to form a fused ring.

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- 9. The compound of claim 1 or 2 wherein L_1 is - X_9NH -wherein X_9 is covalently bonded directly to Z_1 and X_9 is a direct bond or -(CH_2)... wherein m is 1 to 5.
- 10. The compound of each of claims 1, 2 or 3 wherein L, is -CH,CONHCH,-.

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 The compound of claim 3 wherein R, is hydrogen, hydrocarbyl, substituted hydrocarbyl, heteroaryl,

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heterocyclo, halogen, acetamido, guanidino, hydroxy, nitro, amino, amidosulfonyl, acylamido, hydrocarbyloxy, substituted hydrocarbyloxy, hydrocarbylthio, substituted hydrocarbylthio, hydrocarbylthio, hydrocarbylsulfonyl, or substituted hydrocarbylsulfonyl.

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12. The compound of claim 2 having the structure:

Wherein

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 $Z_1,\ Z_2,\ Z_3,\ X_1,\ X_2,\ X_3$ $X_4,\ X_5,\$ and X_6 are as defined in claim 2;

 X_9 is a direct bond or -(CH₂)_u- where m is 1 or 2; and Z_4 is as defined in claim 3.

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- 13. The compound of claim 12 wherein $Z_1,\ Z_2,\ Z_3,\ and\ Z_4$ are as defined in claim 6.
- 14. The compound of each of claims 2, 3 or 12 wherein X_2 is carbon and Z_2 is hydrogen, fluorine, oxygen, or sulfur.

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- 15. The compound of each of claims 2, 3 or 12 wherein X_2 is nitrogen and Z_2 is hydrogen, an electron pair, or a hydrogen bond acceptor.
- 16. The compound of each of claims 2, 3 or 12 wherein X_2 is nitrogen and Z_2 is hydrogen or oxygen.

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17. The compound of each of claims 2, 3 or 12 wherein X_s is carbon optionally substituted with a

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halogen.

18. The compound of each of claims 2, 3 or 12 wherein Z_1 is $-R_{100}C(=NR_{101})NR_{102}R_{100}$, wherein R_{100} is a 6 membered carbocyclic aromatic ring, R_{101} , R_{101} , R_{102} , R_{101} are independently selected from hydrogen, optionally substituted hydrocarbyl, and optionally substituted hetero atoms selected from the group consisting of halogen, oxygen, nitrogen, phosphorous and sulfur.

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19. The compound of each of claims 2, 3 or 12 wherein Z_3 is $-R_{310}C(-NR_{313})NR_{313}R_{313}$, R_{310} is a 6 membered carbocyclic aromatic ring, and at least two of R_{313} , R_{323} , R_{313} are ring atoms of a heterocyclic ring.

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20. The compound of each of claims 2, 3 or 12 wherein Z, is -R₁₀₅C(=NR₁₀₁)NR₁₀₂R₁₀₃, R₁₀₀ is a 6 membered carbocyclic aromatic ring, and at least one of R₁₀₁, R₁₀₂, R₁₀₃ are ring atoms of a heterocyclic ring fused to R₁₀₀.

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21. The compound of claim 20 wherein Z, is benzene substituted with a derivatived amidine which, upon hydrolysis, oxidation, reduction or elimination under physiological conditions yields an amidine group.

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22. The compound of claim 21 wherein Z₄ is a substituted, 6 member, carbocyclic aromatic ring.

23. The compound of each of claims 2, 3, or 12 wherein $\mathbf{Z_4}$ is

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R42 is amino;

Ru is hydrocarbyl, substituted hydrocarbyl, haloen or an optionally substituted hetero atom selected from the group consisting of oxygen, nitrogen, and sulfur; and

R₄₁, R₄₃ and R₄₈ are independently hydrogen, and hydrocarbyl, substituted hydrocarbyl, halogen or an optionally substituted hetero atom selected from the group consisting of oxygen, nitrogen, and sulfur

24. The compound of claim 23 wherein R., is hydrocarbyl, substituted hydrocarbyl, acetamido, alkoxy, hydroxy, amino, alkylsulfonyl, haloalkyl, haloalkoxy, haloalkylthio, carboalkoxy, carboxy, carboxamidoalkyl, or carboxamidoalkylaryl.

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25. The compound of claim 23 wherein each of $R_{41},\ R_{43}$ and R_{45} are hydrogen.

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26. The compound of claim 12 wherein X_9 is a direct bond, Z_1 is selected from the group consisting of cyclopropyl, isopropyl, cyclobutyl, isobutyl, sec-butyl, methyl, ethyl, and phenyl, and Z_3 is benzene substituted with an amidine group.

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 The compound of claim 12 wherein Z, is benzene substituted with a derivatized amidine which, upon

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hydrolysis, oxidation, reduction or elimination under physiological conditions yields an amidine group. 28. The compound of claim 12 wherein X, is a direct bond, Z, is a substituted, 6 member, carbocyclic aromatic ring, Z, is benzene substituted with a derivatized amidine which, upon hydrolysis, oxidation, reduction or elimination under physiological conditions yields an amidine group, and and Z, is selected from the group consisting of cyclopropyl, isopropyl, methyl, ethyl, cyclobutyl, sec-butyl, and phenyl.

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29. The compound of claim 12 or 28 wherein X, is a direct bond, Z, is isopropyl, Z, is benzene substituted with a derivatized amidine which, upon hydrolysis, oxidation, reduction or elimination under physiological conditions yields an amidine group, and Z, is

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R, is amino;

R., is hydrocarbyl, substituted hydrocarbyl, halogen or an optionally substituted hetero atom selected from the group consisting of oxygen, nitrogen, and sulfur; and

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R₁₁, R₁, and R₁₅ are independently hydrogen, hydrocarbyl, substituted hydrocarbyl, halogen or an optionally substituted hetero atom selected from the group consisting of oxygen, nitrogen, and sulfur.

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30. The compound of claim 29 wherein R_{44} is selected

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from the group consisting of hydroxy, alkylsulfonyl, haloalkyl, haloalkoxy, haloalkylthio, carboxamidoalkyl, and carboxamidoalkylaryl.

31. The compound of claim 29 wherein R., is hydrocarbyl, substituted hydrocarbyl, acetamido, alkoxy, hydroxy, amino, alkylsulfonyl, haloalkyl, haloalkoxy, haloalkylthio, carboalkoxy, carboxamidoalkyl, or carboxamidoalkylaryl.

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32. The compound of claim 29 wherein each of $R_{43}\,,\;R_{43}$ and R_{45} is hydrogen.

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wherein Z, comprises a 5 or 6 membered heterocycle or aromatic ring substituted with a derivatized amidine which, upon hydrolysis under physiological conditions, yields an amidine group, the amidine being derivatized with one or more groups selected from carbonyl, thiocarbonyl, imino, enamino, phosphorus, and sulfur.

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34. The compound of each of claims 2, 3, or 12 wherein 2, comprises a 5 or 6 membered heterocycle or aromatic ring substituted with a derivatized amidine which, upon oxidation under physiological conditions yields an amidine group, the amidine being derivatized with one or more groups selected from the groups consisting of (i) optionally substituted hydrocarbyl provided that the carbon atom directly bonded to the amidine is sp³ hybridized, and (ii) aryl.

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35. The compound of each of claims 2, 3, or 12 wherein Z, comprises a 5 or 6 membered heterocycle or aromatic ring substituted with a derivatized amidine which, upon reduction under physiological conditions yields an amidine group, the amidine being derivatized

with one or more hetero atoms selected from the group consisting of oxygen, nitrogen in its most reduced state, and sulfur in its most reduced state. wherein Z, comprises a 5 or 6 membered heterocycle or aromatic ring substituted with a derivatized amidine which, upon elimination under physiological conditions yields an amidine group, the amidine being derivatized with one or more groups selected from the groups consisting of a hydrocarbyl substituted at the beta carbon with carbonyl, sulfonyl, sulfinyl, cyano and nitro or an alkyl group substituted with oxygen, nitrogen, or sulfur at the carbon directly bonded to the amidine group.

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37. The compound of claim 33 wherein Z, is a benzamidine derivative which hydrolyzes under physiological conditions to form benzamidine, the benzamidine derivative having the formula

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R₃₀₁, R₃₀₂, and R₃₀₃ are independently selected from the group consisting of hydrogen, C(=O)R, S(=O)OR, S(=O)SR, S(=O)₂OR, S(=O)₂SR and alkenyl, provided that the carbon atom directly bonded to the amidine is sp² hybridized, provided, however, at least one of R₃₀₁, R₃₀₂, and R₃₀₃ is other than hydrogen;

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R is hydrocarbyl, substituted hydrocarbyl, or heterocyle;

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 $R_{\rm 30c}$ is halogen, hydrogen, hydroxyl, sulfhydryl, alkoxy, and alkylthio;

R_{10s} is oxygen, sulfur, halogen, hydrogen, hydroxyl, sulfhydryl, alkoxy, and alkylthio;

 R_{los} is halogen, hydrogen, hydroxyl, sulfhydryl, alkoxy, and alkylthio; and

R₁₀, is oxygen, sulfur, halogen, hydrogen, hydroxyl, sulfhydryl, alkoxy, and alkylthio.

38. The compound of claim 34 wherein Z, is a benzamidine derivative which oxidizes under physiological conditions to form benzamidine, the benzamidine derivative having the formula

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R₁₀₁, R₁₀₂, and R₁₀₃ are independently selected from the group consisting of hydrogen, optionally substituted hydrocarbyl and aryl, provided, however, (i) at least one of R₁₀₁, R₁₀₂, and R₁₀₃ is other than hydrogen and (ii) the carbon atom directly bonded to the amidine is sp³ hybridized when R₁₀₁, R₁₀₂, and R₁₀₃ is optionally substituted hydrocarbyl;

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 $R_{\rm 3u}$ is halogen, hydrogen, hydroxyl, sulfhydryl, alkoxy, and alkylthio,

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 $R_{\rm 105}$ is oxygen, sulfur, halogen, hydrogen, hydroxyl, sulfhydryl, alkoxy, and alkylthio,

R₁₀₅ is halogen, hydrogen, hydroxyl, sulfhydryl,

alkoxy, and alkylthio; and R_{10} , is oxygen, sulfur, halogen, hydrogen, hydroxyl, sulfhydryl, alkoxy, and alkylthio.

39. The compound of claim 35 wherein Z, is a physiological conditions to form benzamidine, the benzamidine derivative which is reduced under benzamidine derivative having the formula

provided, however, at least one of R, 11, R, 11, and R, 18 R, 11, R, 12, and R, 13, are independently hydrogen, -OR, .SR, -NR, or -N(R), wherein each R is independently optionally substituted hydrocarbyl, or heterocylo, other than hydrogen;

R, is halogen, hydrogen, hydroxyl, sulfhydryl, alkoxy, and alkylthio;

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R₁₀₅ is oxygen, sulfur, halogen, hydrogen, hydroxyl sulfhydryl, alkoxy, and alkylthio;

R, is halogen, hydrogen, hydroxyl, sulfhydryl, alkoxy, and alkylthio; and

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R30, 18 oxygen, sulfur, halogen, hydrogen, hydroxyl, sulfhydryl, alkoxy, and alkylthio.

benzamidine derivative which undergoes an elimination benzamidine, the benzamidine derivative having the The compound of claim 36 wherein Z, is a reaction under physiological conditions to form Formula

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(ii) substituted hydrocarbyl wherein the carbon bonded to the amidine group is substituted with -OR, -SR, -NR, or (iii) substituted alkyl with the carbon atom beta to the R₁₀₁, R₁₀₁, and R₁₀₁ are independently (i) hydrogen, unsaturated electron withdrawing group, provided, at hydrocarbyl, substituted hydrocarbyl or heterocyclo, point of attachment to the amidine group being an -C(0)NRb, -C(0)N(Rb), and each Rb is independently -N(R,), wherein each R is independently -C(O)R,

least one of R301, R302, and R303 is other than hydrogen;

 R_{304} is halogen, hydrogen, hydroxyl, sulfhydryl, alkoxy, and alkylthio;

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R₃₀₅ is oxygen, sulfur, halogen, hydrogen, hydroxyl, R₁₀₆ is halogen, hydrogen, hydroxyl, sulfhydryl, sulfhydryl, alkoxy, and alkylthio;

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R₁₀, is oxygen, sulfur, halogen, hydrogen, hydroxyl, sulfhydryl, alkoxy, and alkylthio. alkoxy, and alkylthio; and

41. The compound of claim 37 wherein R₁₀₁ and R₁₀₅ together with the benzene ring of which R, 18 a substituent form a fused ring.

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42. The compound of claim 38 wherein R_{joi} and R_{jos} together with the benzene ring of which Ryos is a substituent form a fused ring.

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43. The compound of claim 39 wherein R_{101} and R_{105} together with the benzene ring of which R_{105} is a substituent form a fused ring.

44. The compound of claim 40 wherein $R_{\rm joi}$ and $R_{\rm jos}$ together with the benzene ring of which $R_{\rm jos}$ is a substituent form a fused ring.

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45. The compound of claim 41 wherein R_{101} and one of R_{101} and R_{101} together with the nitrogen atoms to which they are bonded form a 5 or 6 membered heterocyclic ring.

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46. The compound of claim 45 wherein the ring atoms are selected from carbon, nitrogen and oxygen.

47. The compound of claim 37 wherein the derivatized amidine upon oxidation, reduction or elimination under physiological conditions yields an amidine group.

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48. The compound of claim 38 wherein the derivatized amidine upon hydrolysis, reduction or elimination under physiological conditions yields an amidine group.

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49. The compound of claim 39 wherein the derivatized amidine upon hydrolysis, oxidation, or elimination under physiological conditions yields an amidine group.

50. The compound of claim 40 wherein the derivatized amidine upon hydrolysis, oxidation, or reduction under physiological conditions yields an amidine group.

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 The compound of each of claims 1-3 or 12 wherein X, is carbon. 52. The compound of each of claims 1-3 or 12 wherein $X_{\rm i}$ is nitrogen.

53. The compound of each of claims 1-3 or 12 wherein X, is carbon.

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54. The compound of each of claims 1-3 or 12 wherein X_1 is nitrogen.

55. The compound of each of claims 1-3 or 12 wherein X, is carbon.

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56. The compound of each of claims 1-3 or 12 wherein $X_{\rm t}$ is carbon.

57. The compound of each of claims 1-3 or 12 wherein $X_{\rm s}$ is nitrogen.

58. The compound of each of claims 1-3 or 12 wherein X, is carbon.

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59. The compound of each of claims 1-3 or 12 wherein X, is nitrogen.

60. The compound of each of claims 1-3 or 12 wherein X₅ is oxygen.

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 The compound of each of claims 1-3 or 12 wherein X, is sulfur. 62. The compound of each of claims 1-3 or 12 wherein $X_{\mathfrak{b}}$ is carbon.

The compound of each of claims 1-3 or 12 wherein X, is nitrogen.

ö The compound of each of claims 1-3 wherein X, is oxygen. 64.

12 0 The compound of each of claims 1-3 wherein X, is sulfur. 65.

The compound of claim 1 having the structure:

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or a pharmaceutically acceptable salt thereof, wherein;

M is N or N→O;

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B is selected from the group consisting of:

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or a carbon adjacent to R^{16} and two atoms from the point of adjacent to the carbon at the point of attachment of said at the other position adjacent to the point of attachment phenyl or heteroaryl ring to A is optionally substituted wherein a nitrogen with a removable hydrogen or a carbon phenyl or a heteroaryl of 5 or 6 ring members, by R12, a nitrogen with a removable hydrogen or a carbon substituted by R11, a nitrogen with a removable hydrogen nitrogen with a removable hydrogen or a carbon adjacent removable hydrogen or a carbon adjacent to R32 and two is optionally substituted by R16, a nitrogen with a to both R¹³ and R¹⁵ is optionally substituted by R¹⁴; attachment is optionally substituted by R35, and a atoms from the point of attachment is optionally

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haloalkyl, wherein each member of group B is optionally (ii) hydrido, trialkylsilyl, C2-C8 alkyl, C3-C8 alkylenyl, C3-C8 alkenyl, C3-C8 alkynyl, and C2-C8

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of the group consisting of R12, R13, R14, R15, and R16; and from the point of attachment of B to A with one or more substituted at any carbon up to and including 6 atoms

atoms from the point of attachment and adjacent to the \mathbb{R}^{12} carbon at the point of attachment of B to A is optionally carbons and a nitrogen adjacent to the carbon atom at the optionally substituted with \mathbb{R}^{10} , a ring carbon or nitrogen point of attachment are optionally substituted with \mathbb{R}^9 or attachment and adjacent to the R^{10} position is optionally substituted with oxo provided that no more than one ring adjacent to the R13 position and two atoms from the point C3-C12 cycloalkyl or C4-C9 saturated of attachment is optionally substituted with R12, a ring position is optionally substituted with \mathbb{R}^{13} , and a ring substituted with R13, a ring carbon other than the ring position and two atoms from the point of attachment is R^{13} , a ring carbon or nitrogen atom adjacent to the R^{9} attachment and adjacent to the R11 and R13 positions is substituted with R11, a ring carbon or nitrogen three heterocyclyl, wherein each ring carbon is optionally carbon is substituted by oxo at the same time, ring carbon or nitrogen three atoms from the point of carbon or nitrogen four atoms from the point of

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R, R10, R11, R12, and R13 are independently selected alkoxyamino, nitro, alkylamino, N-alkyl-N-arylamino, heteroaralkoxy, heterocyclyloxy, heterocyclylalkoxy, cycloalkylalkoxy, aralkoxy, aryloxy, heteroaryloxy, haloacetamido, amidino, guanidino, alkylenedioxy, from the group consisting of hydrido, acetamido, haloalkylthio, alkanoyloxy, alkoxy, cycloalkoxy, alkoxyalkyl, haloalkoxylalkyl, hydroxy, amino, arylamino, aralkylamino, heteroarylamino, heteroaralkylamino, heterocyclylamino, optionally substituted with R34; 30 32

heterocyclylalkylamino, alkylthio, alkylthioalkyl, alkylsulfinyl, arylsulfinyl, aralkylsulfinyl

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alkyl, alkenyl, halo, haloalkyl, haloalkenyl, haloalkoxy, alkylsulfonamido, amidosulfonyl, alkanoyl, haloalkanoyl, heteroarylsulfonyl, alkylsulfonylalkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, cycloalkylsulfinyl, heteroarylsulfinyl, alkylsulfonyl, haloalkoxyalkyl, carboxyalkyl, carboalkoxy, carboxy, arylsulfonyl, aralkylsulfonyl, cycloalkylsulfonyl, hydroxyhaloalkyl, hydroxyalkyl, aminoalkyl, carboxamido, carboxamidoalkyl, and cyano;

R32, R33, R34, R35, and R36 are selected from the group consisting of:

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nydroxy, amino, alkoxyamino, nitro, alkylamino, N-alkylalkoxy, cycloalkoxy, cycloalkylalkoxy, aralkoxy, aryloxy, N-arylamino, arylamino, aralkylamino, heteroarylamino, (i) hydrido, acetamido, haloacetamido, amidino, guanidino, alkylenedioxy, haloalkylthio, alkanoyloxy, heterocyclylalkoxy, alkoxyalkyl, haloalkoxylalkyl, neterocyclylalkylamino, alkylthio, alkylthioalkyl, heteroaryloxy, heteroaralkoxy,heterocyclyloxy, neteroaralkylamino, heterocyclylamino, 12 20

alkyl, alkenyl, halo, haloalkyl, haloalkenyl, haloalkoxy, alkylsulfonamido, amidosulfonyl, alkanoyl, haloalkanoyl, cycloalkylsulfinyl, heteroarylsulfinyl, alkylsulfonyl, heteroarylsulfonyl, alkylsulfonylalkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, haloalkoxyalkyl, carboxyalkyl, carboalkoxy, carboxy, arylsulfonyl, aralkylsulfonyl, cycloalkylsulfonyl, carboxamido, carboxamidoalkyl, and cyano; and alkylsulfinyl, arylsulfinyl, aralkylsulfinyl, hydroxyhaloalkyl, hydroxyalkyl, aminoalkyl,

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 $(W^7)_{rr}$ - $(CH(R^{15}))_{pa}$, and $(CH(R^{15}))_{pa}$ - $(W^7)_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 6, and W? (R7)NC(0), (R7)NC(S), and N(R7) with the proviso that no A is selected from the group consisting of a bond, is selected from the group consisting of 0, S, C(0),

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more than one of the group consisting of rr and pa is 0 at the same time;

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R' is selected from the group consisting of hydrido

hydroxy, and alkyl;

R15 is selected from the group consisting of hydrido, hydroxy, halo, alkyl, and haloalkyl;

W 18 NH or NOH;

Ja is N or C-Xº;

Jb is N or C-R1;

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X° is selected from the group consisting of:

haloalkyl, haloalkoxy, haloalkylthio, amino, aminoalkyl, alkylamino, amidino, hydroxy, hydroxyamino, alkoxy, hydroxyalkyl, alkoxyamino, thiol, and alkylthio; hydrido, alkyl, alkenyl, cyano, halo,

R1 is selected from the group consisting of: (i) hydrido, alkyl, alkenyl, cyano, halo,

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haloalkyl, haloalkoxy, haloalkylthio, amino, aminoalkyl, alkylamino, amidino, hydroxy, hydroxyamino, alkoxy, hydroxyalkyl, alkoxyamino, thiol, and alkylthio;

(ii) taken with X^0 or R^2 to form -W=X-Y=Z-; wherein -W=X-Y=Z- forms an aryl or C5-C6 heteroaryl; and

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taken with X° or R' bonded together to form C5-C8 cycloalkenyl ring or a partially saturated C5-C8 heterocyclyl ring, wherein said cycloalkenyl ring or more of the group consisting of $R^9,\ R^{10},\ R^{11},\ R^{12},\ and\ R^{13};$ heterocyclyl ring is optionally substituted with one or

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group consisting of $C(R^9)$, $C(R^{10})$, $C(R^{11})$, $C(R^{12})$, N, $N(R^{10})$ W, X, Y, and Z is O or S, with the further proviso that and Z is independently selected to be a bond when one of no more than one of W, X, Y, and Z is optionally O or S, and with the additional proviso that no more than three W, X, Y, and Z are independently selected from the O, S, and a bond with the proviso that one of W, X, Y, of W, X, Y, and Z are optionally N or N(R10);

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 \mathbf{Z}^{0} is selected from the group consisting of:

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wherein g and p are integers independently selected from 0 through 3 and W° is selected from the group consisting selected from 1 through 3, and $(CH(\mathbb{R}^{41}))_{\mathfrak{g}}-W^{\mathfrak{g}}-(CH(\mathbb{R}^{42}))_{\mathfrak{p}}$ a bond, (CR*1R*2), wherein q is an integer of O, S, C(O), S(O), N(R⁴¹), and ON(R⁴¹); and

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pyridine ring and W^{22} is optionally substituted with one or more substituents selected from the group consisting of tetrahydrofuranyl, wherein 2° is directly bonded to the consisting of CR"=CR", 1,2-cyclopropyl, 1,2-cyclobutyl, independently 0 or 1 and W22 is selected from the group pyrrolidinyl, 2,4-pyrrolidinyl, 2,5-pyrrolidinyl, 3,4piperidinyl, 1,2-pyrrolidinyl, 1,3-pyrrolidinyl, 2,3-1,2-cyclohexyl, 1,3-cyclohexyl, 1,2-cyclopentyl, 1,3-(ii) (CH(R41)),-W22-(CH(R42)), wherein e and h are piperidinyl, 2,4-piperidinyl, 2,6-piperidinyl, 3,4cyclopentyl, 2,3-morpholinyl, 2,4-morpholinyl, 2,6morpholinyl, 3,4-morpholinyl, 3,5-morpholinyl, 1,2piperazinyl, 1,3-piperazinyl, 2,3-piperazinyl, 2,6piperazinyl, 1,2-piperidinyl, 1,3-piperidinyl, 2,3tetrahydrofuranyl, 2,5-tetrahydrofuranyl, and 3,4pyrrolidinyl, 2,3-tetrahydrofuranyl, 2,4-R3, R10, R11, R12, and R13;

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R'1 and R'2 are independently selected from the group consisting of amidino, hydroxyamino, hydrido, hydroxy, amino, and alkyl;

Q is selected from the group consisting of:

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by R³, a nitrogen with a removable hydrogen or a carbon at optionally substituted by R¹³, a nitrogen with a removable the other position adjacent to the point of attachment is hydrogen or a carbon adjacent to R' and two atoms from the adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to Z° is optionally substituted wherein a nitrogen with a removable hydrogen or a carbon (1) phenyl or a heteroaryl of 5 or 6 ring members, nitrogen with a removable hydrogen or a carbon adjacent point of attachment is optionally substituted by \mathbb{R}^{10} , a

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removable hydrogen or a carbon adjacent to both $R^{{\rm i}\,{\rm b}}$ and $R^{{\rm 13}}$ optionally substituted by \mathbb{R}^{12} , and a nitrogen with a to R13 and two atoms from the point of attachment is is optionally substituted by R11; and

(ii) hydrido with the proviso that 2° is selected from other than a bond;

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K is selected from the group consisting of:

CR**R*b; and Ŧ (ii) (CH(R14)),-T wherein j is 0 or 1 and T is a bond or N(R') with the proviso that (CH(R'')), is bonded to the phenyl ring;

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R** and R*b are independently selected from the group consisting of halo, hydrido, hydroxyalkyl, alkyl, alkoxyalkyl, alkylthioalkyl, and haloalkyl;

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(i) E¹, with the proviso that K is CR48R4b, wherein B¹ $S(0)_2N(H)$, $N(H)S(0)_2$, $S(0)_2N(H)C(0)$, and $C(0)N(H)S(0)_2$; and single bond, C(0)N(H), (H)NC(0), C(S)N(H), (H)NC(S), is selected from the group consisting of a covalent Eo is selected from the group consisting of:

(ii) \mathbb{E}^2 , with the proviso that K is $(CH(\mathbb{R}^{14}))_{j}$ -T, wherein E' is selected from the group consisting of C(O)N(H), (H)NC(O), C(S)N(H), (H)NC(S), $S(O)_2N(H)$, $N(H) S(O)_2$, $S(O)_2 N(H) C(O)$, and $C(O) N(H) S(O)_2$;

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R14 is selected from the group consisting of hydrido, halo, alkyl, and haloalkyl;

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Yo is selected from the group consisting of:

substituted by Q°, a carbon two or three contiguous atoms optionally substituted by Ri6, and another carbon adjacent from the point of attachment of $\mathbb{Q}^{\mathfrak{s}}$ to said phenyl or said attachment of Q° is optionally substituted by R17, another (1) phenyl or a heteroaryl of 5 or 6 ring members, optionally substituted by R^{10} , a carbon adjacent to \mathbb{Q}^{b} is wherein one carbon of said phenyl or said heteroaryl is substituted by Q^b, a carbon adjacent to the point of carbon adjacent to the point of attachment of Q' is heteroaryl to said phenyl or said heteroaryl is

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to Q^b is optionally substituted by R¹⁹;

(ii) Y^{AT} wherein Y^{AT} is $Q^{b}-Q^{\bullet}$; and

(iii) Q^{a} - Q^{a} wherein Q^{a} is $(CH(R^{14}))_{a}$ - W^{2} - $(CH(R^{15}))_{h}$, wherein e and h are independently 1 or 2 and W^{2} is CR^{4a} - CR^{4a} - CR^{4b} , with the proviso that $(CH(R^{14}))_{a}$ is bonded to E^{a} ;

R¹⁷ and R¹⁹ are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, nitro, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, alkenyl, haloalkoxy, hydroxyalkyl, aminoalkyl, haloalkoxyalkyl, aminoalkyl, haloalkoxyalkyl, carboalkoxy, and cyano;

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 R^{16} and R^{19} are independently selected from the group consisting of:

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(1) hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, nitro, alkyyamino, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, alkenyl, halo, haloalkoxy, hydroxyalkyl, aminoalkyl, haloalkoxyalkyl, carboalkoxy, and cyano,

(ii) $NR^{20}R^{21}$, $N(R^{26})C(NR^{25})N(R^{23})$ (R^{24}), and $C(NR^{25})NR^{21}R^{24}$, with the proviso that R^{16} , R^{19} , and Q^b are not

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simultaneously hydrido;

Ob is selected from the group consisting of NR²⁰R²¹, aminoalkyl, hydrido, N(R²⁶)C(NR²⁵)N(R²¹) (R²⁴), and C(NR²⁵)NR²¹R²⁴, with the proviso that no more than one of

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aminoalkyl, hydrido, N(R²⁵)C(NR²⁵)N(R²¹), and C(NR²⁵)NR²³R²⁴, with the proviso that no more than one of R²⁰ and R²¹ is selected from the group consisting of hydroxy, amino, alkylamino, and dialkylamino at the same time, with the further proviso that no more than one of R²¹ and R²¹ is selected from the group consisting of hydroxy, amino, alkylamino, and dialkylamino at the same time; R²⁰, R²¹, R²¹, R²¹, R²³, and R²⁴ are independently

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R²⁰, R²¹, R²¹, R²⁴, R²⁵, and R²⁶ are independently selected from the group consisting of hydrido, alkyl, hydroxy, aminoalkyl, amino, dialkylamino, alkylamino, and hydroxyalkyl;

Q° is selected from the group consisting of a bond

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 $(CR^3 R^{14})_b$ wherein b is an integer selected from 1 through 4, and $(CH(R^{14}))_c$ -W¹- $(CH(R^{15}))_d$ wherein c and d are integers independently selected from 1 through 3 and W¹ is selected from the group consisting of $C(O)N(R^{14})$, $(R^{14})NC(O)$, S(O), $S(O)_2N(R^{14})$, $N(R^{14})S(O)_2$, and $N(R^{14})$, with the proviso that R^{14} is selected from other than halo when directly bonded to N, and with the additional proviso that $(CR^{27}R^{24})_b$, and $(CH(R^{14}))_c$, are bonded to B^o ;

R¹⁷ is independently selected from the group consisting of hydrido, alkyl, and haloalkyl;

R¹⁸ is selected from the group consiting of hydrido, alkyl, haloalkyl, aroyl or heteroaroyl, wherein R¹⁸ is optionally substituted with one or more substituents selected from the group consisting of R¹⁸, R¹⁷, R¹⁸, and R¹⁹.

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67. The compound of claim 66 having the structure:

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or a pharmaceutically acceptable salt thereof, wherein; M is N or N \rightarrow O;

B is selected from the group consisting of:

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wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to A is optionally substituted by R¹², the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R¹⁵, a carbon adjacent to R¹⁷ and two atoms from the carbon at the point of attachment is optionally substituted by R¹⁵, a carbon adjacent to R¹⁵ and two atoms from the carbon at the point of attachment is optionally substituted by R¹⁵, and any carbon adjacent to both R¹⁵ and R¹⁵ is optionally substituted by R¹⁵, and any carbon adjacent to both R¹⁷ and R¹⁵ is optionally substituted by R¹⁸;

(ii) hydrido, trialkylsilyl, C2-C8 alkyl, C3-C8 alkylenyl, C3-C8 alkenyl, C3-C8 alkynyl, and C2-C8 haloalkyl, wherein each member of group B is optionally substituted at any carbon up to and including 6 atoms from the point of attachment of B to A with one or more of the group consisting of R¹³, R¹³, R¹⁴, R¹⁵, and R¹⁵, and

adjacent to the \mathbb{R}^{12} position is optionally substituted with optionally substituted with R11, a ring carbon or nitrogen carbons and a nitrogen adjacent to the carbon atom at the optionally substituted with \mathbb{R}^{10} , a ring carbon or nitrogen carbon at the point of attachment of B to A is optionally point of attachment are optionally substituted with $\ensuremath{\text{R}}^9$ or point of attachment is optionally substituted with \mathbb{R}^{12} , a substituted with oxo provided that no more than one ring atom adjacent to the R¹³ position and two atoms from the ring carbon or nitrogen atom three atoms from the point position and two atoms from the point of attachment is R13, and a ring carbon or nitrogen atom four atoms from substituted with R13, a ring carbon other than the ring R^{13} , a ring carbon or nitrogen atom adjacent to the R^{9} the point of attachment and adjacent to the \mathbb{R}^{11} and \mathbb{R}^{33} heterocyclyl, wherein each ring carbon is optionally carbon is substituted by oxo at the same time, ring (iii) C3-C12 cycloalkyl or a C4-C9 saturated atom three atoms from the point of attachment and of attachment and adjacent to the R10 position is positions is optionally substituted with \mathbb{R}^{14} ;

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R, R10, R11, R12, and R13 are independently selected from the group consisting of hydrido, acetamido, haloacetamido, alkoxyamino, alkanoyl, haloalkanoyl, amidino, guanidino, alkylenedioxy, haloalkylthio, alkoxy, cycloalkylalkoxy, aralkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, heteroaralkoxy, mino, alkylamino, N-alkyl-N-arylamino, arylamino, aralkylamino, heteroarylamino, heteroaralkylamino, heteroarylamino,

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heterocyclylalkylamino, alkylthio, alkylaulfinyl, arylaulfinyl, arylaulfinyl, aralkylaulfinyl, cycloalkylaulfinyl, heteroarylaulfinyl, alkylaulfamido, alkylaulfonyl, arylaulfonyl, aralkylaulfonyl, cycloalkylaulfonyl, aralkyl, cycloalkylaulfonyl, alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, carboalkoxy, carboxy, carboxy, carboxylkyl, carboxyalkyl, and cyano;

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A is bond or (CH(R1s))_{ps}-(W²)_{rr} wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W² is selected from the group consisting of 0, S, C(0), (R²)NC(0), (R²)NC(S), and N(R²), with the proviso that W² is bonded to the N(H) on the pyridine ring,

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 R^{γ} is selected from the group consisting of hydrido, hydroxy and alkyl; $R^{15} \text{ is selected from the group consisting of hydrido,} \\ \text{hydroxy, halo, alkyl, and haloalkyl;}$

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Ja is Nor C-Xº;

Jb 18 N or C-R1;

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x° is independently selected from the group consisting of hydrido, alkyl, cyano, halo, haloalkyl, haloalkoxy, amino, aminoalkyl, alkylamino, amidino, hydroxy, hydroxyamino, alkoxy, hydroxyalkyl, alkoxyamino, thiol, and alkylthio;

R' is selected from the group consisting of:

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(i) hydrido, alkyl, cyano, halo, haloalkyl, haloalkoxy, amino, aminoalkyl, alkylamino, amidino, hydroxy, hydroxyamino, alkoxy, hydroxyalkyl, alkoxyamino, thiol, and alkylthio;

(ii) taken with X^0 or R^2 to form -W=X-Y=Z-; wherein -W=X-Y=Z- forms an aryl or heteroaryl of 5 or 6 ringmembers; and

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(iii) taken with X° or R² bonded together to form C5-C8 cycloalkenyl ring or a partially saturated C5-C8 heterocyclyl ring, wherein said cycloalkenyl ring or

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more of the group consisting of $R^9,\ R^{10},\ R^{11},\ R^{12},\ and\ R^{13},$ heterocyclyl ring is optionally substituted with one or

O, S and a bond with the proviso that one of W, X, Y, and group consisting of $C(\mathbb{R}^9)$, $C(\mathbb{R}^{10})$, $C(\mathbb{R}^{11})$, $C(\mathbb{R}^{12})$, N, $N(\mathbb{R}^{10})$, X, Y, and Z is O or S, with the further proviso that no W, X, Y, and Z are independently selected from the Z is independently selected to be a bond when one of W, more than one of W, X, Y, and Z is optionally selected additional proviso that no more than three of W, X, Y, from the group consisting of O and S, and with the and Z are optionally N or N(R10);

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R2 is Z0-Q;

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Z° is selected from the group consisting of:

independently selected from 0 through 3 and W° is selected from the group consisting of O, S, C(O), S(O), N(R 41), and (i) a bond, $(CR^{41}R^{42})_q$ wherein q is 1 or 2, and (CH(R41))g-W0-(CH(R42))p wherein g and p are integers ON (R41); and

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syridine ring and W22 is optionally substituted with one or more substituents selected from the group consisting of consisting of CR*1=CR*2, 1,2-cyclopropyl, 1,2-cyclobutyl, cetrahydrofuranyl, wherein 2° is directly bonded to the independently 0 or 1 and W22 is selected from the group pyrrolidinyl, 2,4-pyrrolidinyl, 2,5-pyrrolidinyl, 3,4-1,2-cyclohexyl, 1,3-cyclohexyl, 1,2-cyclopentyl, 1,3-(ii) (CH(R41)),-Wa2-(CH(R42)), wherein e and h are piperidinyl, 1,2-pyrrolidinyl,1,3-pyrrolidinyl, 2,3piperidinyl, 2,4-piperidinyl, 2,6-piperidinyl, 3,4piperazinyl, 1,2-piperidinyl, 1,3-piperidinyl, 2,3morpholinyl, 3,4-morpholinyl, 3,5-morpholinyl, 1,2piperazinyl, 1,3-piperazinyl, 2,3-piperazinyl, 2,6cyclopentyl, 2,3-morpholinyl, 2,4-morpholinyl,2,6tetrahydrofuranyl, 2,5-tetrahydrofuranyl, and 3,4pyrrolidinyl, 2,3-tetrahydrofuranyl, 2,4-

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R*1 and R*2 are independently selected from the group

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consisting of hydrido, hydroxy, alkyl, and amino;

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Q is selected from the group consisting of:

optionally substituted by R', the other carbon adjacent to substituted by R¹², and any carbon adjacent to both R¹⁰ and from the carbon at the point of attachment is optionally substituted by R10, a carbon adjacent to R13 and two atoms from the carbon at the point of attachment is optionally phenyl or a heteroaryl of 5 or 6 ring members, substituted by R13, a carbon adjacent to R9 and two atoms wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to 2° is the carbon at the point of attachment is optionally R12 is optionally substituted by R11; and

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(ii) hydrido with the proviso that Zo is other than a pouq;

K is selected form the group consisting of

CR*R*b;

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- (ii) $(CH(R^{14}))_3$ -T wherein j is 0 or 1 and T is a bond or N(R7) with the proviso that (CH(R14)); is bonded to the
 - phenyl ring;

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R** and R*b are independently selected from the group consisting of hydrido, hydroxyalkyl, alkyl, alkoxyalkyl, alkylthioalkyl, and haloalkyl;

R14 is hydrido or halo,

E° is selected from the group consisting of:

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- covalent single bond, C(O)N(H), (H)NC(O), S(O),N(H), and E'wherein E' is selected from the group consisting of a E1, with the proviso that K is CR48R4b, is N(H)S(O); and
- 18 (ii) E², with the proviso that K is (CH(R¹⁴)),-T, E'wherein E' is selected from the group consisting of C(O)N(H), (H)NC(O), C(S)N(H), (H)NC(S), S(O),N(H), N(H)S(O),, S(O),N(H)C(O), and C(O)N(H)S(O);

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(1) phenyl or a heteroaryl of 5 or 6 ring members, wherein one carbon of said phenyl or said heteroaryl is Y° is selected from the group consisting of:

substituted by Q^a , a carbon two or three atoms from the point of attachment of Q^a to said phenyl or said heteroaryl is substituted by Q^b , a carbon adjacent to the point of attachment of Q^a is optionally substituted by R^{17} , another carbon adjacent to the point, of attachment of Q^a is optionally substituted by R^{18} , a carbon adjacent to Q^b is optionally substituted by R^{18} , and another carbon adjacent to Q^b is optionally substituted by R^{18} ;

w

(ii) YAT wherein YAT is Qb-Q"; and

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(iii) Qb-Q** wherein Q** is (CH(R'*)),e-W²-(CH(R'\$)),b,
wherein e and h are independently 1 or 2 and W² is
CR**=CR** with the proviso that (CH(R'**)), is bonded to B°;

R¹⁷ and R¹⁸ are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkoxyamino, alkylamino, alkylsulfinyl, alkylsulfinyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano;

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Ri* and Ri* are selected from the group consisting of:

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(i) hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkoxyamino, alkylamino, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, haloalkyl, haloalkyl, haloalkyl, aminoalkyl, and cyano; and

(ii) $NR^{20}R^{21}$, $N(R^{26})C(NR^{25})N(R^{23})$ (R^{24}), and $C(NR^{25})NR^{23}R^{24}$, with the proviso that R^{16} , R^{19} , and Q^{p} are not simultaneously hydrido;

25

Q^b is selected from the group consisting of NR²⁰K, hydrido, N(R²⁶)C(NR²⁹)N(R²¹) (R²¹), and C(NR²¹)NR²¹R²¹, with the proviso that no more than one of R²⁰ and R²¹ is selected from the group consisting of hydroxy, amino, alkylamino, and dialkylamino at the same time, with the further proviso that no more than one of R²¹ and R²¹ is selected from the group consisting of hydroxy, amino, alkylamino, and dialkylamino at the same time;

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R²⁰, R²¹, R²³, R²⁴, R²⁵, and R²⁶ are independently

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selected from the group consisting of hydrido, alkyl, hydroxy, amino, alkylamino and dialkylamino;

Q* is selected from the group consisting of a bond, (CR¹R¹¹), wherein b is an integer selected from 1 through 4, and (CH(R¹⁴))_c-W¹-(CH(R¹⁵))_d wherein c and d are integers independently selected from 1 through 3 and W¹ is selected from the group consisting of C(O)N(R¹⁴), (R¹⁴)NC(O), S(O), S(O), S(O), R(O), N(R¹⁴), N(R¹⁴)S(O), and N(R¹⁴), with the proviso that R¹⁴ is selected from other than halo when directly bonded to N, and with the additional proviso that (CR¹³R³¹), and (CR¹³R³¹), and (CR¹R³¹), are bonded to E°;

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R¹⁷ is independently selected from the group consisting of hydrido, alkyl, and haloalkyl;

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R¹⁸ is selected from the group conisting of hydrido, alkyl, haloalkyl, aroyl or heteroaroyl, wherein R¹⁸ is optionally substituted with one or more substituents selected from the group consisting of R¹⁶, R¹⁷, R¹⁸, and

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68. The compound of claim 67 or a pharmaceutically acceptable salt thereof, wherein;

M is N or N→O;

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B is selected from the group consisting of hydrido, trialkylsilyl, C2-C8 alkyl, C3-C8 alkylenyl, C3-C8 alkynyl, and C2-C8 haloalkyl, wherein each member of group B is optionally substituted at any carbon up to and including 6 atoms from the point of attachment of B to A with one or more of the group consisting of R³³, R³⁴, R³⁵, and R³⁶;

25

R¹², R¹³, R¹⁴, R¹⁵, and R¹⁶ are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkoxy, hydroxy, amino, alkylamino, alkylthio, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, hydroxyhaloalkyl, carboalkoxy, carboxi, carboxamido, cyano, and Q^b;

A is (CH(R15)) p.-W' wherein pa is an integer selected consisting of O, S, and N(R') wherein R' is hydrido or from 0 through 3 and W' is selected from the group alkyl; R15 is selected from the group consisting of hydrido, hydroxy, halo, alkyl, and haloalkyl;

Ja is N or C-Xº;

Jb is N or C-R1;

hydroxy, hydroxyamino, alkoxy, hydroxyalkyl, alkoxyamino, R^1 and X^0 are independently selected from the group consisting of hydrido, alkyl, cyano, halo, haloalkyl, haloalkoxy, amino, aminoalkyl, alkylamino, amidino, thiol, and alkylthio;

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R' is Z°-Q;

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R' and R' are independently selected from the group Z^0 is a bond or $(CR^{4.1}R^{42})_{\mathfrak{q}}$ wherein q is 1 or $Z_{\mathfrak{p}}$ consisting of hydrido, hydroxy, and amino;

optionally substituted by R, the other carbon adjacent to substituted by \mathbb{R}^{12} , and any carbon adjacent to both \mathbb{R}^{10} and R^{12} is optionally substituted by R^{11} , with the proviso that from the carbon at the point of attachment is optionally from the carbon at the point of attachment is optionally substituted by R10, a carbon adjacent to R13 and two atoms Q is phenyl or a heteroaryl of 5 or 6 ring members, substituted by R13, a carbon adjacent to R9 and two atoms wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to \mathbf{z}^{o} is the carbon at the point of attachment is optionally Q is other than a phenyl when Z° is a bond;

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amidino, guanidino, alkylenedioxy, haloalkylthio, alkoxy, heterocyclylalkoxy, hydroxy, amino, alkylamino, N-alkyl- $R^9,\ R^{10},\ R^{11},\ R^{12},\ and\ R^{13}$ are independently selected haloacetamido, alkoxyamino, alkanoyl, haloalkanoyl, cycloalkoxy, cycloalkylalkoxy, aralkoxy, aryloxy, from the group consisting of hydrido, acetamido, heteroaryloxy, heteroaralkoxy,heterocyclyloxy,

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heteroarylsulfonyl, amidosulfonyl, alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, N-arylamino, arylamino, aralkylamino, heteroarylamino, hydroxyhaloalkyl, aminoalkyl, carboalkoxy, carboxy, heterocyclylalkylamino, alkylthio, alkyleulfinyl, arylsulfinyl, aralkylsulfinyl, cycloalkylsulfinyl, heteroarylBulfinyl, alkylBulfamido, alkylBulfonyl, arylsulfonyl, aralkylsulfonyl, cycloalkylsulfonyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, heteroaralkylamino, heterocyclylamino 20

consisting of hydrido, hydroxyalkyl, alkyl, alkoxyalkyl, K is CHR" wherein R" is selected from the group carboxyalkyl, carboxamido, and cyano; alkylthioalkyl, and haloalkyl;

Yo is selected from the group consisting of: C(O)N(H), (H)NC(O), $(R^7)NS(O)_2$, and $S(O)_2N(R^7)$;

E' is selected from the group consisting of a bond,

12

heteroaryl ring is substituted by $\mathbb{Q}^{\flat},$ a carbon adjacent to the point of attachment of Q" is optionally substituted by $R^{17},\,$ another carbon adjacent to the point of attachment of substituted by Q°, a carbon two or three contiguous atoms Q° is optionally substituted by R¹8, a carbon adjacent to (i) phenyl or a heteroaryl of 5 or 6 ring members, wherein one carbon of said phenyl or said heteroaryl is Q is optionally substituted by R16, and another carbon from the point of attachment of Q° to the phenyl or adjacent to Qb is optionally substituted by R19; and

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wherein e and h are integers independently selected from (ii) Q^b - Q^{**} wherein Q^{**} is $(CH(R^{14}))_a$ - W^2 - $(CH(R^{15}))_h$, 1 through 2 and W2 is CR40-CH with the proviso that (CH(R14)), is bonded to E0;

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haloalkylthio, alkoxy, hydroxy, amino, alkoxyamino, lower R17 and R18 are independently selected from the group alkylamino, alkylthio, alkyleulfinyl, alkyleulfonyl, consisting of hydrido, amidino, guanidino, carboxy, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl,

haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano;

 $R^{16} \ and \ R^{19}$ are selected from the group consisting of:

(1) hydrido, amidino, guanidino, carboxy, naloalkylthio, alkoxy, hydroxy, amino, alkoxyamino, low

haloalkylthio, alkoxy, hydroxy, amino, alkoxyamino, lower alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano; and

(ii) $NR^{20}R^{21}$, $N(R^{26})C(NR^{25})N(R^{23})$ (R^{24}) , and $C(NR^{25})NR^{23}R^{24}$ with the proviso that R^{16} , R^{19} , and Q^b are not simultaneously hydrido;

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Q^b is selected from the group consisting of NR²⁰R²¹, hydrido, N(R²⁴)C(NR²³)N(R²³) (R²⁴), and C(NR²⁵)NR²³R²⁴, with the proviso that no more than one of R²⁰ and R²¹ is selected from the group consisting of hydroxy, amino, alkylamino, and dialkylamino at the same time and with the further proviso that no more than one of R²³ and R²⁴ is selected from the group consisting of hydroxy, amino, alkylamino, and dialkylamino at the same time;

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R²⁰, R²¹, R²¹, R²⁴, and R²⁶ are independently selected from the group consisting of hydrido, alkyl, hydroxy, amino, alkylamino and dialkylamino;

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 Q^{\bullet} is selected from the group consisting of a bond, $(CR^{17}R^{10})_{b}$ wherein b is an integer selected from 1 through 3, and

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(CH(R¹⁴))_c-W¹-(CH(R¹⁵))_d wherein c and d are independently 1 or 2 and W¹ is selected from the group consisting of C(0)N(R¹⁴), (R¹⁴)N(0), S(0), S(0), S(0)₂, S(0)₂, N(R¹⁴), N(R¹⁴)S(0)₂, and N(R¹⁴), with the proviso that R¹⁴ is selected from other than halo when directly bonded to N and with the further proviso that (CR¹⁷R¹⁸)₅, and (CH(R¹⁴))_c are bonded to E⁰;

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R¹⁴ is selected from the group consisting of hydrido, alkyl, and haloalkyl;

R¹⁷ is independently selected from the group

consisting of hydrido, alkyl, and haloalkyl; R³⁸ is selected from the group consisting of hydrido,

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alkyl, haloalkyl, aroyl and heteroaroyl.

69. The compound of claim 68 having the structure:

or a pharmaceutically acceptable salt thereof, wherein; M is N or N \rightarrow O;

B is selected from the group consisting of hydrido, trialkylsilyl, C2-C4 alkyl, C3-C5 alkylenyl, C3-C4 alkynel, and C2-C4 haloalkyl, wherein each member of group B is optionally substituted at any carbon up to and including 3 atoms from the point of attachment of B to A with one or more of the group consisting of R²²,

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R12, R13, and R14 are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkoxy, hydroxy, amino, alkoxyamino, alkylamino, alkylthio, amidosulfonyl, alkyl, halo, haloalkyl, hydroxyalkyl, hydroxyhaloalkyl, carboalkoxy, carboxamido, and cyano;

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A is (CH(R¹⁵))_{pa}-N(R⁷) wherein pa is an integer selected from 0 through 2 and R⁷ is hydrido or alkyl;
R¹⁵ is selected from the group consisting of hydrido, halo, alkyl, and haloalkyl;

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Ja is Nor C-X';

Jb is N or C-R1;

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R¹ and X⁰ are independently selected from the group consisting of hydrido, alkyl, cyano, halo, haloalkyl, haloalkoxy, amino, aminoalkyl, alkylamino, amidino, hydroxy, hydroxyamino, alkoxy, hydroxyalkyl, alkoxyamino, thiol, and alkylthio;

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R2 is Z0-Q;

Z° is a bond or CH2;

optionally substituted by R', the other carbon adjacent to substituted by R12, and any carbon adjacent to both R10 and from the carbon at the point of attachment is optionally substituted by R¹⁰, a carbon adjacent to R¹¹ and two atoms from the carbon at the point of attachment is optionally substituted by R13, a carbon adjacent to R9 and two atoms Q is phenyl or a heteroaryl of 5 or 6 ring members wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to Z° is the carbon at the point of attachment is optionally R12 is optionally substituted by R11;

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R, R11, and R13 are independently selected from the group consisting of hydrido, hydroxy, amino, amidino, guanidino, alkylamino, alkylthio, alkylsulfonamido, alkylsulfinyl, alkylsulfonyl, amidosulfonyl, alkyl, hydroxyhaloalkyl, carboxy, carboxamido, and cyano; alkoxy, halo, haloalkyl, haloalkoxy, hydroxyalkyl,

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R10 and R12 are independently selected from the group neterocyclylalkylamino, alkylsulfonamido, amidosulfonyl, carboxyalkyl, carboxamido, halo, haloalkyl, and cyano; cycloalkylsulfonyl, heteroarylsulfonyl, hydroxyalkyl, amidino, guanidino, alkyl, aryl, aralkyl, cycloalkyl, alkylamino, arylamino, aralkylamino, heteroarylamino, hydroxyhaloalkyl, aminoalkyl, carboalkoxy, carboxy, arylsulfinyl, aralkylsulfinyl, cycloalkylsulfinyl, heteroarylsulfinyl, arylsulfonyl, aralkylsulfonyl, cycloalkylalkyl, heteroaryl, heterocyclyl, alkoxy, cycloalkoxy, cycloalkylalkoxy, aralkoxy, aryloxy, consisting of hydrido, acetamido, haloacetamido, neterocyclylalkoxy, hydroxy, amino, alkoxyamino, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, heteroaralkylamino, heterocyclylamino,

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Y° is phenyl or a heteroaryl of 5 or 6 ring members, wherein one carbon of said phenyl or said heteroaryl is

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point of attachment of Q^{ullet} is optionally substituted by $\mathbb{R}^{17},$ heteroaryl is substituted by Qb, a carbon adjacent to the another carbon adjacent to the point of attachment of \mathbb{Q}^{\bullet} is optionally substituted by \mathbb{R}^{18} , a carbon adjacent to $\mathbb{Q}^{\mathtt{b}}$ atoms from the is optionally substituted by R^{16} , and another carbon point of attachment of Q° to said phenyl or said adjacent to \mathbb{Q}^b is optionally substituted by \mathbb{R}^{19} ; substituted by Q*, a carbon two or three

R17 and R18 are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoy1, alky1, halo, haloalky1, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano;

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 R^{16} and R^{19} are selected from the group consisting of: alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, haloalkanoy1, alky1, halo, haloalky1, haloalkoxy, (i) hydrido, amidino, guanidino, carboxy,

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(11) NR20R21, N(R26)C(NR25)N(R23)(R24), and C(NR25)NR13R24, with the proviso that R^{16} , R^{19} , and Q^b are not hydroxyalkyl, aminoalkyl, and cyano; simultaneously hydrido;

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hydrido, $C(NR^{25})NR^{23}R^{24}$, and $N(R^{26})C(NR^{25})N(R^{23})$ (R^{24}), with the provise that no more than one of \mathbb{R}^{20} and \mathbb{R}^{21} is hydroxy at the same time and with the further proviso that no more \mathbb{Q}^{\flat} is selected from the group consisting of $NR^{20}R^{21},$ than one of R13 and R24 is hydroxy at the same time;

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selected from the group consisting of hydrido, alkyl, and R21, R21, R24, R35, and R26 are independently hydroxy;

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Q* is selected from the group consisting of a bond, CH, and CH,CH, 70. The compound of claim 69 or a pharmaceutically acceptable salt thereof, wherein;

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M is N or N→O;

B is selected from the group consisting of ethyl, 2-proppnyl, 2-propynyl, isopropyl, -CH₂CH₂CH₃-. -CH₂CH₃CH₃-. butyl, 2-butenyl, 3-butenyl, 2-butynyl, secbutyl, tert-butyl, 1sobutyl, 2-methylpropenyl, 2,2,2-trifluoroethyl, 3,3,3-trifluoropropyl, and 2,2-difluoropropyl, wherein each member of group B is optionally substituted at any carbon up to and including 3 atoms from the point of attachment of B to A with one or more of the group consisting of R¹³, R¹³, and R¹⁴;

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group consisting of hydrido, amidino, guanidino, carboxy, methoxy, ethoxy, isopropoxy, propoxy, hydroxy, amino, methoxyamino, ethoxyamino, acetamido, trifluoroacetamido, N-methylamino, dimethylamino, N-ethylamino, methylthio, ethylthio, tsopropylthio, trifluoromethyl, nentylthio, 2,2-trifluoromethyl, trifluoromethyl

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pentafluoroethy1, 2,2,2-trifluoroethy1, trifluoromethoxy,
1,1,2,2-tetrafluoroethoxy, fluoro, chloro, bromo,
amidosulfony1, N-methylamidosulfony1, N,N-

amidosulfonyl, N-methylamidosulfonyl, N,Ndimethylamidosulfonyl, hydroxymethyl, 1-hydroxyethyl, 2hydroxyethyl,

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2,2,2-trifluoro-1-hydroxyethyl, methoxycarbonyl, ethoxycarbonyl, amidocarbonyl, N-methylamidocarbonyl, N,N-dimethylamidocarbonyl, and cyano;

N.N-dimethylamidocarbonyl, and cyano;
A is selected from the group consisting of a bond,

Ja is N or C-X0;

and N(CH3);

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Jb is N or C-R1;

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R¹ and X° are independently selected from the group consisting of hydrido, hydroxy, amino, amidino, hydroxyamino, aminomethyl, 1-aminoethyl, methylamino, dimethylamino, cyano, methyl, ethyl, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, methoxy, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, methoxyamino, methylthlo, ethylthio, trifluoromethoxy,

1,1,2,2-tetrafluoroethoxy, fluoro, chloro, and bromo;

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R2 is Z0-Q;

Z° is a bond or CH2;

carbon adjacent to R13 and two atoms from the carbon at the adjacent to the carbon at the point of attachment of said carbon adjacent to R' and two atoms from the carbon at the phenyl or heteroaryl ring to \mathbf{z}^{o} is optionally substituted pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, point of attachment is optionally substituted by \mathbb{R}^{12} , and 4-pyridazinyl, and 1,3,5-triazin-2-yl, wherein a carbon point of attachment is optionally substituted by R^{10} , a Q is selected from the group consisting of phenyl, point of attachment is optionally substituted by R11, a 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3pyrazoly1, 2-thiazoly1, 3-isoxazoly1, 5-isoxazoly1, 2pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-pyrazolyl, 4by R', the other carbon adjacent to the carbon at the any carbon adjacent to both R10 and R12 is optionally pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2substituted by R11;

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R⁹, R¹¹, and R¹³ are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, methyl, ethyl, propyl, isopropyl, methoxy, ethoxy, isopropoxy, propoxy, hydroxy, amino, N-methylamino, N, N-dimethylamino, N-ethylamino, methylthio, ethylthio, isopropylthio, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, chloro, bromo, methanesulfonamido, amidosulfonyl, N-methylamidosulfonyl, N-dimethylamidosulfonyl, 1-hydroxyethyl, 2-hydroxyethyl, 2,2,2-trifluoro-1-hydroxyethyl, amidocarbonyl, N-methylamidocarbonyl, N-dimethylamidocarbonyl, and

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R¹⁰ and R¹² are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, carboxymethyl, methyl, ethyl, propyl, isopropyl, methoxy,

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1-aminoethyl, 2-aminoethyl, N-methylamino, dimethylamino, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 2,2,2ethoxycarbonyl, amidocarbonyl, N-methylamidocarbonyl, N-ethylamino, methanesulfonamido, amidosulfonyl, Nmethylamidosulfonyl, N,N-dimethylamidosulfonyl, ethoxy, isopropoxy, propoxy, hydroxy, amino, trifluoro-1-hydroxyethyl, methoxycarbonyl, methoxyamino, ethoxyamino, acetamido, trifluoroacetamido, aminomethyl,

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N-benzylamidosulfonyl, N-(2chlorobenzyl) amidosulfonyl, N-isopropylamidocarbonyl, N-N, N-dimethylamidocarbonyl, N-benzylamidocarbonyl, N-(2cyclobutylamidocarbonyl, N-cyclopentylamidocarbonyl, trifluoromethylbenzyl) amidocarbonyl, N-(1phenylethyl)amidocarbonyl, N-(1-methyl-1chlorobenzyl) amidocarbonyl, N-(3fluorobenzyl) amidocarbonyl, N-(2phenylethyl) amidocarbonyl, 15 10

cyclopentoxy, benzyl, benzyloxy, 4-bromo-3-fluorophenoxy, -chloro-3-ethylbenzylamino, 4-chloro-3-ethylphenylamino, 3-bromobenzyloxy, 4-bromobenzyloxy, 4-bromobenzylamino, chlorobenzyl, 4-chlorophenoxy, 4-chloro-3-ethylphenoxy, cyclohexylmethoxy, 4-trifluoromethycyclohexylmethoxy, 5-bromopyrid-2-ylmethylamino, 4-butoxyphenamino, 3-3-chlorobenzyloxy, 4-chlorobenzyloxy, 4-20 25

fluoro, chloro, bromo, cyano, cyclobutoxy, cyclohexdxy,

chlorophenylaulfonyl, 5-chloropyrid-3-yloxy,2-cyanopyrid-3-yloxy, 2,3-difluorobenzyloxy, 2,4-difluorobenzyloxy, difluoromethoxybenzyloxy, 2,3-difluorophenoxy, 2,4-3,4-difluorobenzyloxy, 2,5-difluorobenzyloxy, 3,5chlorobenzyleulfonyl, 4-chlorophenylamino, 4difluorophenoxy, 3,5-difluorobenzyloxy, 4difluorophenoxy, 2,5-difluorophenoxy, 3,5-30

ethoxyphenoxy, 4-ethylbenzyloxy, 3-ethylphenoxy, 4ethylaminophenoxy, 3-ethyl-5-methylphenoxy, 4dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 4-35

dimethylphenoxy, 3,4-dimethylphenoxy, 3,4-

3-trifluoromethoxyphenoxy, 4-trifluoromethoxyphenoxy, 3fluorobenzyloxy, 2-fluoro-3-trifluoromethylbenzyloxy, 3methylphenoxy, 4-isopropylbenzyloxy, 3-isopropylphenoxy, trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, trifluoromethylbenzyloxy, 4-trifluoromethylbenzyloxy, fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2isopropylphenoxy, 4-isopropylphenoxy, 4-isopropyl-3phenylethyl, 2-phenylethylamino, phenylsulfonyl, 3fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4trifluoromethylphenoxy, 4-isopropylbenzyloxy, 3-4-isopropylphenoxy, 4-isopropyl-3-methylphenoxy, phenylamino, 1-phenylethoxy, 2-phenylethoxy, 2fluoro-5-trifluoromethylbenzyloxy, 4-fluoro-2trifluoromethylbenzyloxy, 2-fluorophenoxy, 4trifluoromethylbenzyloxy, 4-fluoro-3-12 10

trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-2,4-bis-trifluoromethylbenzyloxy, 3trifluoromethylthiobenzyloxy, 4-

2,3,5-trifluorophenoxy, 3-pentafluoroethylphenoxy, 3trifluoromethylthiobenzyloxy, 2,3,4-trifluorophenoxy, (1,1,2,2-tetrafluoroethoxy) phenoxy, and 3trifluoromethylthiophenoxy;

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3-Q^b-6-Q"-2-R¹⁶-5-R¹⁸-4-R¹⁹pyridine, 2-Q^b-5-Q"-3-R¹⁶-6-Y° is selected from the group consisting of: 1-Qb-4-Q8-2-R16-3-R17-5-R18-6-R19benzene, 2-Qb-5-Q-6-R17-4-R18-3-R18pyridine, R¹⁰pyrazine, 25

2-Qb-5-Qe-4-R17-6-R18pyrimidine, 5-Qb-2-Qe-4-R16-6-3-Q^b-5-Q^a-4-R¹⁶-2-R¹⁹thiophene, 2-Q^b-5-Q^a-3-R¹⁶-4-R19primidine, R17thiophene, 30

3-Qb-6-Q-2-R10-5-R10-4-R19pyridazine,

3-Q^b-5-Q*-4-R¹⁶-2-R¹⁹pyrrole, 2-Q^b-5-Q*-3-R¹⁶-4-R¹⁷pyrrole, 3-Qb-5-Qa-4-R16-2-R19furan, 2-Qb-5-Qa-3-R16-4-R17furan, 4-Qb-2-Q"-5-R19imidazole, 2-Qb-4-Q"-5-R17imidazole, 35

3-Q°-5-Q°-4-R¹¹isoxazole, 5-Q°-3-Q°-4-R¹⁵isoxazole, 2-Q°-5-Q°-4-R¹⁰pyrazole, 4-Q°-2-Q°-5-R¹ºthiazole, and 2-Q°-5-Q°-4-R¹'thiazole, R¹⁷ and R¹⁸ are independently selected from the group consisting of hydrido, methyl, ethyl, isopropyl, propyl, carboxy, amidino, guanidino, methoxy, ethoxy, isopropoxy, propoxy, hydroxy, amino, aminomethyl, 1-aminoethyl, 2-aminoethyl, N-methylamino, dimethylamino, N-ethylamino, methylthio, ethylthio, isopropylthio,

trifluoromethylthio, methylsulfinyl, ethylsulfinyl, methylsulfonyl, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3-pentafluoroptopyl, trifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, chloro, bromo, hydroxymethyl, 1-hydroxyethyl, and cyano;

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 R^{16} and R^{19} are selected from the group consisting of:

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 (i) hydrido, methyl, ethyl, isopropyl, propyl, carboxy, amidino, guanidino, methoxy, ethoxy, isopropoxy, propoxy, hydroxy, amino, aminomethyl, 1-aminoethyl, 2aminoethyl, N-methylamino, dimethylamino, N-ethylamino, methylthio, ethylthio, isopropylthio,

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trifluoromethylthio, methylsulfinyl, ethylsulfinyl, methylsulfonyl, ethylsulfonyl, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3-pentafluoropropyl, trifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, chloro, bromo, hydroxymethyl, 1-hydroxyethyl, and cyano; and

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1-hydroxyethyl, 2-hydroxyethyl, and cyano; and (ii) NR²⁰R²¹, N(R²⁶)C(NR²⁵)N(R²³) (R²⁴), and C(NR²⁵)NR²³R²⁴

with the proviso that R^{16} , R^{19} , and Q^b are not simultaneously hydrido; $Q^b \text{ is selected from the group consisting of NR^{20}R^{21},}$

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hydrido, C(NR²³)NR²¹R²⁴, and N(R²⁴)C(NR²³)N(R²¹) (R²⁴), with the proviso that no more than one of R²⁰, R²¹, R²¹, and R²⁴ can be hydroxy, when any two of the group consisting of R²⁰, R²¹, R²¹, and R²⁴ are bonded to the same atom and with the further proviso that said Q² group is bonded directly

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to a carbon atom;

 R^{20} , R^{21} , R^{21} , R^{21} , and R^{26} are independently selected from the group consisting of hydrido, methyl, ethyl, propyl, butyl, isopropyl, and hydroxy;

 Q^{\bullet} is selected from the group consisting of a bond, CH,, and CH_2CH_2 .

71. The compound of claim 70 having the structure:

or a pharmaceutically acceptable salt thereof, wherein; M is N or $N\!\to\!0$;

A is selected from the group consisting of CH,N(CH,), CH,N(CH,CH,), CH,CH,N(CH,), and CH,CH,N(CH,CH,);

Jb is N or C-R';

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R¹ and X° are independently selected from the group consisting of hydrido, hydroxy, amino, amidino, hydroxyamino, aminomethyl, 1-aminoethyl, methylamino, dimethylamino, cyano, methyl, ethyl, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, methoxy, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl,

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R' is Z^0-Q ; Z^0 is a bond or CH_2 ;

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methoxyamino, methylthio, ethylthio, trifluoromethoxy,

1,1,2,2-tetrafluoroethoxy, fluoro, chloro, and bromo;

O is selected from the group consisting of phenyl, 2-thienyl, 3-thienyl, 2-turyl, 3-furyl, 2-pyrrolyl, 3-pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-pyrazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 2-pyridyl, 3-pyridyl, 2-pyrzinyl, 2-pyrimidinyl, 4-pyrimidinyl, 2-pyrzimidinyl, 3-pyridazinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, 4-pyridazinyl, 3-pyridazinyl, and 1,3,5-triazin-2-yl, wherein a carbon

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carbon adjacent to R13 and two atoms from the carbon at the carbon adjacent to R' and two atoms from the carbon at the adjacent to the carbon at the point of attachment of said point of attachment is optionally substituted by \mathbb{R}^{12} , and phenyl or heteroaryl ring to Z° is optionally substituted point of attachment is optionally substituted by $R^{10},\ a$ point of attachment is optionally substituted by R^{13} , a by R°, the other carbon adjacent to the carbon at the any carbon adjacent to both R10 and R12 is optionally substituted by R11;

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group consisting of hydrido, amidino, guanidino, carboxy, isopropylthio, trifluoromethyl, pentafluoroethyl, 2,2,2-R, R11, and R11 are independently selected from the N, N-dimethylamino, N-ethylamino, methylthio, ethylthio, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 2,2,2chloro, bromo, methanesulfonamido, amidosulfonyl, Ntrifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, methylamidocarbonyl, N,N-dimethylamidocarbonyl, and isopropoxy, propoxy, hydroxy, amino, N-methylamino, methyl, ethyl, propyl, isopropyl, methoxy, ethoxy, methylamidosulfonyl, N,N-dimethylamidosulfonyl, trifluoroethyl, 2,2,3,3,3-pentafluoropropyl, trifluoro-1-hydroxyethyl, amidocarbonyl, Ncyano;

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methanesulfonamido, amidosulfonyl, N-methylamidosulfonyl, R10 and R12 are independently selected from the group carboxymethyl, methyl, ethyl, propyl, isopropyl, methoxy, N.N-dimethylamidosulfonyl, hydroxymethyl, 1-hydroxyethyl, aminoethyl, N-methylamino, dimethylamino, N-ethylamino, consisting of hydrido, amidino, guanidino, carboxy, methoxycarbonyl, ethoxycarbonyl, amidocarbonyl, Nmethylamidocarbonyl, N,N-dimethylamidocarbonyl, Ntrifluoroacetamido, aminomethyl, 1-aminoethyl, 2-2-hydroxyethyl, 2,2,2-trifluoro-1-hydroxyethyl, ethoxy, isopropoxy, propoxy, hydroxy, amino, methoxyamino, ethoxyamino, acetamido,

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methylphenoxy, 4-isopropylbenzyloxy, 3-isopropylphenoxy

isopropylphenoxy, 4-isopropylphenoxy, 4-isopropyl-3-

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fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-

trifluoromethylbenzyloxy, 2-fluorophenoxy, 4-

trifluoromethylbenzyloxy, 4-fluoro-2-

trifluoromethylbenzyloxy, 4-fluoro-3-

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fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4trifluoromethylphenoxy, 4-isopropylbenzyloxy, 3-

benzylamidocarbonyl, N-(2-chlorobenzyl)amidocarbonyl,

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phenylethyl) amidocarbonyl, N-benzylamidosulfonyl, N-(2cyclopentoxy, benzyl, benzyloxy, 4-bromo-3-fluorophenoxy, 4-chloro-3-ethylbenzylamino, 4-chloro-3-ethylphenylamino chlorobenzyl) amidosulfonyl, N-isopropylamidocarbonyl, Ndimethylbenzyloxy, 4-ethoxyphenoxy, 4-ethylbenzyloxy, 3fluoro, chloro, bromo, cyano, cyclobutoxy, cyclohexoxy, 3-bromobenzyloxy, 4-bromobenzyloxy, 4-bromobenzylamino, chlorobenzyl, 4-chlorophenoxy, 4-chloro-3-ethylphenoxy, cyclohexy1methoxy, 4-trifluoromethycyclohexy1methoxy, cyclobutylamidocarbonyl, N-cyclopentylamidocarbonyl, 5-bromopyrid-2-ylmethylamino, 4-butoxyphenamino, 3difluorobenzyloxy, 4-difluoromethoxybenzyloxy, 2,3chlorophenylsulfonyl, 5-chloropyrid-3-yloxy, 2cyanopyrid-3-yloxy, 2,3-difluorobenzyloxy, 2,4difluorobenzyloxy, 3,4-difluorobenzyloxy, 2,5chlorobenzylsulfonyl, 4-chlorophenylamino, 4ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5methylphenoxy, 4-fluorobenzyloxy, 2-fluoro-3difluorobenzyloxy, 3,5-difluorophenoxy, 3,5dimethylphenoxy, 3,4-dimethylbenzyloxy, 3,5-N-(3-fluorobenzyl)amidocarbonyl, N-(2difluorophenoxy, 2,4-difluorophenoxy, 2,5difluorophenoxy, 3,5-dimethylphenoxy, 3,4trifluoromethylbenzyl) amidocarbonyl, N-(1phenylethyl)amidocarbonyl, N-(1-methyl-1-3-chlorobenzyloxy, 4-chlorobenzyloxy, 4trifluoromethylbenzyloxy, 3-fluoro-5-'n 10 15 20 25

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3-trifluoromethoxyphenoxy, 4-trifluoromethoxyphenoxy, 3trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, trifluoromethylbenzyloxy, 4-trifluoromethylbenzyloxy, phenylethyl, 2-phenylethylamino, phenylsulfonyl, 3-4-isopropylphenoxy, 4-isopropyl-3-methylphenoxy, phenylamino, 1-phenylethoxy, 2-phenylethoxy, 2-2,4-bis-trifluoromethylbenzyloxy, 3-

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rifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-:rifluoromethylthiobenzyloxy, 2,3,4-trifluorophenoxy, trifluoromethylthiobenzyloxy, 4-

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2,3,5-trifluorophenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, and 3crifluoromethylthiophenoxy;

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[-Qb-4-Q*-2-R16-3-R17-5-R18-6-R19benzene, 2-Qb-5-Q*-6-R17-4-R18-1-R'9pyridine, 3-Q^-6-Q"-2-R'6-5-R'8-4-R'9pyridine, 2-Q^2-5-Q"-3.6-4-R¹⁷furan, 3-Q^b-5-Q°-4-R¹⁶-2-R¹⁹pyrrole, 2-Q^b-5-Q°-3-R¹⁶-4-3-R16-6-R18pyrazine, 3-Qb-6-Q6-2-R18-5-R18-4-R19pyridazine, 2-3-4-R17thiophene, 3-Qb-5-Q-4-R16-2-R19furan, 2-Qb-5-Q-3-R¹⁹pyrimidine, 3-Q^b-5-Q^e-4-R¹⁶-2-R¹⁹thiophene, 2-Q^b-5-Q^e-3-R17imidazole, 3-Qb-5-Q"-4-R16isoxazole, 5-Qb-3-Q"-4- Y^{o} is selected from the group consisting of: R¹⁶180xazole, 2-Q^b-5-Q^a-4-R¹⁶pyrazole, 4-Q^b-2-Q^a-5-R¹⁷pyrrole, 4-Q^b-2-Q^e-5-R¹⁹imidazole, 2-Q^b-4-Q^e-5-2-5-0"-4-R17-6-R18pyrimidine, 5-Q2-2-Q"-4-R18-6- R^{19} thiazole, and 2- Q^{b} -5- Q^{a} -4- R^{17} thiazole;

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R16, R17, R18, and R19 are independently selected from isopropyl, propyl, amidino, guanidino, methoxy, ethoxy, aminoethyl, 2-aminoethyl, N-methylamino, dimethylamino, isopropoxy, propoxy, hydroxy, amino, aminomethyl, 1-M-ethylamino, methylthio, ethylthio, isopropylthio, trifluoromethylthio, methylsulfinyl, ethylsulfinyl, pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3methylsulfonyl, ethylsulfonyl, trifluoromethyl, the group consisting of hydrido, methyl, ethyl, pentafluoropropyl, trifluoromethoxy, 1,1,2,2-

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tetrafluoroethoxy, fluoro, chloro, bromo, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, and cyano;

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O is selected from the group consisting of NR²⁰R²¹,

further proviso that said Q° group is bonded directly to a hydroxy, when any two of the group consisting of R^{20} , R^{21} , C(NR²⁵)NR²³K, and N(R²⁶)C(NR²⁵)N(R²³)(R²⁴), with the proviso R23 , and R24 are bonded to the same atom, and with the that no more than one of R20, R11, R11, and R24 can be carbon atom;

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selected from the group consisting of hydrido, methyl, R^{10} , R^{21} , R^{23} , R^{24} , R^{25} , and R^{26} are independently ethyl, propyl, butyl, isopropyl, and hydroxy;

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O' is selected from the group consisting of a bond, CH2, and CH2CH2. The compound of claim 71 or a pharmaceutically acceptable salt thereof, wherein;

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M is N→O;

A is selected from the group consisting of CH,N(CH,), CH₂N(CH₂CH₃), CH₂CH₃N(CH₃), and CH₂CH₃N(CH₃CH₃);

Jb is C-R1;

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R and X are independently selected from the group hydroxyamino, aminomethyl, methylamino, cyano, methyl, trifluoromethyl, methoxy, hydroxymethyl, methoxyamino, methylthio, trifluoromethoxy, fluoro, and chloro; consisting of hydrido, hydroxy, amino, amidino,

R2 18 Z0-Q;

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Z° is a bond or CH2;

benzylamidocarbonyl)phenyl, 3-amino-5-benzylphenyl, 3-Q is selected from the group consisting of 3-amidocarbony1-5-aminopheny1, 3-amino-5-(Namino-5-(2-phenylethyl)phenyl, 3-amino-5-

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benzylaminophenyl, 3-amino-5-(2-phenylethylamino)phenyl, 3-amino-5-benzyloxyphenyl, 3-amino-5-(2phenylethoxy) phenyl, 3-amino-5-(N-(2-

chlorobenzyl)amidocarbonyl)phenyl, 3-amino-5-(N-(3-

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trifluoromethylbenzyl)amidocarbonyl)phenyl, 3-amino-5-(Nsyanophenyl, 3,5-diaminophenyl, 3-dimethylaminophenyl, 2methyl-1-phenylethyl)amidocarbonyl)phenyl, 3-amino-5-(Nmethoxyphenyl, 3-methoxyphenyl, 3-methoxyaminophenyl, 3rrifluoromethylphenyl, 2-trifluoromethylphenyl, 5-aminomethylphenyl, 5-amino-2-methylthiophenyl, 3-aminophenyl, cyclohexylamidocarbonyl)phenyl, 5-amino-2-fluorophenyl, 3-carboxyphenyl, 3-carboxy-5-hydroxyphenyl, 3-amino-5-(1-phenylethyl) amidocarbonyl) phenyl, 3-amino-5-(N-(1methylaminophenyl, 2-methylphenyl, 3-methylphenyl, 4nethylphenyl, phenyl, 3-trifluoroacetamidophenyl, 3-2-thienyl, 5-amino-3-thienyl, 3-bromo-2-thienyl, 3fluorobenzyl)amidocarbonyl)phenyl, 3-amino-5-(N-(2nethoxycarbonylphenyl, 3-amidinophenyl, 3-amino-2carboxyphenyl, 3-chlorophenyl, 2-chlorophenyl, 3fluorophenyl, 3-fluorophenyl, 2-hydroxyphenyl, 3chlorobenzyl)amidosulfonyl)phenyl, 3-amino-5-(Nhydroxyphenyl, 3-methanesulfonylaminophenyl, 2isobutylamidocarbonyl)phenyl, 3-amino-5-(N-(2cyclopentylamidocarbonyl)phenyl, 3-amino-5-(Nmethoxycarbonylphenyl, 2-methylaminophenyl, 3cyclobutylamidocarbonyl)phenyl, 3-amino-5-(Nbenzylamidosulfonyl)phenyl, 3-amino-5-(N-(2isopropylamidocarbonyl)phenyl, 3-amino-5-(N-3-amino-5-hydroxymethylphenyl, 5-amino-3propylamidocarbonyl) phenyl, 3-amino-5-(Nbutyl) amidocarbonyl) phenyl, 3-amino-5-(Nethylamidocarbonyl)phenyl, 3-amino-5-(N-

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1-Q2-4-Q"-2-R16-3-R17-5-R18-6-R19benzene, 2-Q2-5-Q"-6-R17-4-R18- R^{16} and R^{19} are independently selected from the group 3-R19pyridine, 3-Qb-6-Q8-2-R18-5-R18-4-R19pyridine, 3-Qb-5-Q8-4-R16-2-R19thiophene, and 2-Q^-5-Q-3-R16-4-R17thiophene; Yo is selected from the group consisting of: pyridyl, 4-pyridyl, 2-thienyl, and 3-thienyl;

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methoxy, methylamino, hydroxy, hydroxymethyl, fluoro, consisting of hydrido, amidino, amino, aminomethyl,

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chloro, and cyano;

R17 and R18 are independently selected from the group consisting of hydrido, fluoro, chloro, hydroxy, hydroxymethyl, amino, carboxy, and cyano;

Qb is C(NR25) NR23R24;

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R23, R24, and R23 are independently selected from the group consisting of hydrido and methyl;

acceptable salt thereof wherein the compound is selected The compound of claim 72 or a pharmaceutically 2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3from the group consisting of: 73.

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aminophenyl] - 6-[N,N-dimethylhydrazino]-1-

oxypyridinyl]]acetamide;

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2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3aminophenyl]-6-[N-ethyl-N-methylhydrazino]-1oxypyridinyl]]acetamide;

2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3aminophenyl]-5-chloro-6-[N,N-dimethylhydrazino]-1oxypyridinyl]]acetamide;

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aminophenyl]-5-chloro-6-[N-ethyl-N-methylhydrazino]-1-2-{2-{N-[{4-aminoiminomethylphenyl}methyl}-3-{3oxypyridinyl]]acetamide;

2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3,5diaminophenyl] - 6-[N, N-dimethylhydrazino] -1oxypyridinyl]]acetamide;

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2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3,5-2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3,5diaminophenyl]-6-[N-ethyl-N-methylhydrazino]-1oxypyridinyl]]acetamide;

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2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3,5diaminophenyl]-5-chloro-6-[N,N-dimethylhydrazino]-1oxypyridinyl]]acetamide;

diaminophenyl]-5-chloro-6-[N-ethyl-N-methylhydrazino]-1oxypyridinyl]]acetamide;

2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3amino-5-carboxyphenyl]- 6-[N,N-dimethylhydrazino]-1oxypyridinyl]]acetamide, 2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3amino-5-carboxyphenyl]-6-[N-ethyl-N-methylhydrazino]-1oxypyridinyl]]acetamide;

2-[2-[N-[[4-aminoiminomethyl]phenyl]methyl]-3-[3amino-5-carboxyphenyl]-5-chloro-6-[N,Ndimethylhydrazino]-1-oxypyridinyl]]acetamide;

2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3amino-5-carboxyphenyl]-5-chloro-6-[N-ethyl-Nmethylhydrazino]-1-oxypyridinyl)]acetamide;

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metnyinydrazinol - 1-0xypyriddinyi) ocetaminos;
2- [2- [N- [[4-aminoiminomethylphenyl]methyl] - 3- [3-amino-5- (N-benzylamidocarbonyl) phenyl] - 6- [N,N-dimethylhydrazino] - 1-0xypyridinyl] acetamide;

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2-[2-[N-[(4-aminoiminomethylphenyl]methyl]-3-[3-amino-5-(N-benzylamidocarbonyl)phenyl]-6-[N-ethyl-N-methylhydrazino]-1-oxypyridinyl)]acetamide;

2-[2-[N-[(4-aminoiminomethylphenyl]methyl]-3-[3-amino-5-(N-benzylamidocarbonyl)phenyl]-5-chloro-6-[N,N-dimethylhydrazino]-1-oxypyridinyl]acetamide;

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2-[2-[N-[[4-aminoiminomethylphenyl]methyl]-3-[3-amino-5-(N-benzylamidocarbonyl)phenyl]-5-chloro-6-[N-ethyl-N-methylhydrazino]-1-oxypyridinyl]]acetamide.

74. The compound of claim 67 having the structure:

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or a pharmaceutically acceptable salt thereof, wherein; M is N or N \rightarrow O;

B is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of

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attachment of said phenyl or heteroaryl ring to A is optionally substituted by R¹², the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R¹⁸, a carbon adjacent to R²⁹ and two atoms from the carbon at the point of attachment is optionally substituted by R²⁹, a carbon adjacent to R²⁸ and two atoms from the carbon at the point of attachment is optionally substituted by R²⁹, and any carbon adjacent to both R²⁹ and R²⁹ is optionally substituted by R²⁹;

from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkoxy, hydroxy, amino, alkylamino, alkylthio, amidosulfonyl, alkyl, halo, haloalkyl, haloalkyl, haloaky, hydroxyalkyl, hydroxyhaloalkyl, carboalkoxy, carboxamido, cyano, and Q^b;

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A is a bond or $(CH(R^{15}))_{pa}-(W^2)_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W² is $(R^2)NC(0)$ or $N(R^2)$;

hydroxy and alkyl;
R¹⁵ is selected from the group consisting of hydrido, halo, alkyl, and haloalkyl;

R' is selected from the group consisting of hydrido,

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Ja is Nor C-X';

Jb is N or C-R1;

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R¹ and X° are independently selected from the group consisting of hydrido, hydroxy, hydroxyamino, amidino, amino, cyano, hydroxyalkyl, alkoxy, alkyl, alkylamino, aminoalkyl, alkylthio, alkoxyamino, haloalkyl,

haloalkoxy, and halo;

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R² is Z°-Q;

 Z^o is selected from the group consisting of a bond, $CH_2, CH_2CH_1,\ W^o-(CH(R^{42}))_p$ wherein p is 0 or 1 and W^o is selected from the group consisting of 0, S, and $N(R^{41})_r$

R'1 and R'3 are independently hydrido or alkyl; Q is phenyl or a heteroaryl of 5 or 6 ring members,

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optionally substituted by R³, the other carbon adjacent to substituted by R^{12} , and any carbon adjacent to both R^{19} and substituted by R10, a carbon adjacent to R13 and two atoms from the carbon at the point of attachment is optionally from the carbon at the point of attachment is optionally substituted by R13, a carbon adjacent to R3 and two atoms wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to Z° is the carbon at the point of attachment is optionally R12 is optionally substituted by R11;

R, R11, and R13 are independently selected from the group consisting of hydrido, hydroxy, amino, amidino, guanidino, alkylamino, alkylthio, alkylsulfonamido, alkyleulfinyl, alkyleulfonyl, amidosulfonyl, alkyl, ydroxyhaloalkyl, carboxy, carboxamido, and cyano; alkoxy, halo, haloalkyl, haloalkoxy, hydroxyalkyl,

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R10 and R12 are independently selected from the group neterocyclylalkylamino, alkylsulfonamido, amidosulfonyl, carboxyalkyl, carboxamido, halo, haloalkyl, and cyano; amidino, guanidino, alkyl, aryl, aralkyl, cycloalkyl, alkylamino, arylamino, aralkylamino, heteroarylamino, cycloalkylsulfonyl, heteroarylsulfonyl, hydroxyalkyl, hydroxyhaloalkyl, aminoalkyl, carboalkoxy, carboxy, arylsulfinyl, aralkylsulfinyl, cycloalkylsulfinyl, cycloalkylalkyl, heteroaryl, heterocyclyl, alkoxy, heteroarylsulfinyl, arylsulfonyl, aralkylsulfonyl, cycloalkoxy, cycloalkylalkoxy, aralkoxy, aryloxy, consisting of hydrido, acetamido, haloacetamido, neterocyclylalkoxy, hydroxy, amino, alkoxyamino, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, heteroaralkylamino, heterocyclylamino,

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heteroaryl is substituted by Q^b, a carbon adjacent to the Yo is phenyl or a heteroaryl of 5 or 6 ring members, substituted by Q*, a carbon two or three atoms from the wherein one carbon of said phenyl or said heteroaryl is point of attachment of Q° to said phenyl or said

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point of attachment of Q° is optionally substituted by R¹7, is optionally substituted by $R^{1\theta},\ a\ carbon\ adjacent to\ Q^{b}$ another carbon adjacent to the point of attachment of Q is optionally substituted by \mathbb{R}^{16} , and another carbon adjacent to Qb is optionally substituted by R19;

R" and R" are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, alkylthio, alkyleulfinyl, alkyleulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano;

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R16 and R19 are selected from the group consisting of:

haloalkylthio, alkoxy, hydroxy, amino, alkylamino, alkylthio, alkylgulfinyl, alkylgulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, (i) hydrido, amidino, guanidino, carboxy, hydroxyalkyl, aminoalkyl, and cyano; and

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(11) NR20R21 or C(NR25)NR21R2, with the proviso that R16, R19, and Q are not simultaneously hydrido;

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with the further proviso that no more than one of \mathbb{R}^{23} and hydrido, and C(NR25)NR29R24, with the proviso that no more Qb is selected from the group consisting of NR'9R'1, than one of R20 and R21 is hydroxy at the same time and R24 is hydroxy at the same time;

from the group consisting of hydrido, alkyl, and hydroxy; R20, R21, R21, R21, and R25 are independently selected Q' is selected from the group consisting of a bond, CH2, and CH3CH3.

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75. The compound of claim 74 or a pharmaceutically acceptable salt thereof, wherein;

M is N or N-O)

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B is selected from the group consisting of phenyl, 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3pyrazoly1, 2-thiazoly1, 3-isoxazoly1, 5-isoxazoly1, 2pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-pyrazolyl, 4-

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pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl,
4-pyridazinyl, and 1,3,5-triazin-2-yl, wherein a carbon
adjacent to the carbon at the point of attachment of said
phenyl or heteroaryl ring to A is optionally substituted
by R¹³, the other carbon adjacent to the carbon at the
point of attachment is optionally substituted by R¹⁴, a
carbon adjacent to R¹² and two atoms from the carbon at the
point of attachment is optionally substituted by R¹³, a
carbon adjacent to R¹⁴ and two atoms from the carbon at the
point of attachment is optionally substituted by R¹³, and
any carbon adjacent to both R¹³ and R¹⁵ is optionally
substituted by R¹⁴;

S

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R¹³, R¹³, R¹³, R¹³, and R¹⁸ are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, methoxy, ethoxy, isopropoxy, propoxy, hydroxy, amino, methoxyamino, ethoxyamino, acetamido, trifluoroactamido, N-methylamino, dimethylamino, N-ethylamino, isopropylthio, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3-pentafluoropropyl, trifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, chloro, bromo, amidosulfonyl, N-methylamidosulfonyl, N-dimethylamidosulfonyl, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 2,2,2-trifluoro-1-hydroxyethyl, methoxycarbonyl, ethoxycarbonyl, amidocarbonyl, N-methylamidocarbonyl, cyano, and Q^b;

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Ja is Nor C-X';

Jb is N or C-R1;

R' and X° are independently selected from the group consisting of hydrido, hydroxy, amino, amidino, hydroxyamino, aminomethyl, 1-aminoethyl, methylamino,

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dimethylamino, cyano, methyl, ethyl, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, methoxy, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, methoxyamino, methylthio, ethylthio, trifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, chloro, and bromo; R² is Z°-Q;

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 Z^{o} is selected from the group consisting of a bond, $CH_{2},\ CH_{2}CH_{2},\ O,\ S,\ NH,\ N(CH_{3}),\ OCH_{2},\ SCH_{2},\ N(H)CH_{3},\ and$

N (CH₃) CH₂;

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carbon adjacent to R13 and two atoms from the carbon at the adjacent to the carbon at the point of attachment of said carbon adjacent to R' and two atoms from the carbon at the phenyl or heteroaryl ring to Z° is optionally substituted point of attachment is optionally substituted by $R^{12},\ and$ pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, 4-pyridazinyl, and 1,3,5-triazin-2-yl, wherein a carbon Q is selected from the group consisting of phenyl, point of attachment is optionally substituted by R13, a point of attachment is optionally substituted by \mathbb{R}^{10} , a 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3pyrazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 2pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-pyrazolyl, 4by R', the other carbon adjacent to the carbon at the any carbon adjacent to both R10 and R12 is optionally pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-

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R, R11, and R13 are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, methyl, ethyl, propyl, isopropyl, methoxy, ethoxy, isopropoxy, propoxy, hydroxy, amino, N-methylamino, N.N-dimethylamino, N-ethylamino, methylthio, ethylthio, isopropylthio, trifluoromethyl, pentafluoroethyl, 2,2,3,3,3-pentafluoropropyl, trifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, chloro, bromo, methanesulfonamido, amidosulfonyl, N-methylamidosulfonyl, N-dimethylamidosulfonyl,

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substituted by R11;

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hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 2,2,2methylamidocarbonyl, N,N-dimethylamidocarbonyl, and trifluoro-1-hydroxyethyl, amidocarbonyl, N-

cyano;

w

carboxymethyl, methyl, ethyl, propyl, isopropyl, methoxy, methanesulfonamido, amidosulfonyl, N-methylamidosulfonyl, N, N-dimethylamidosulfonyl, hydroxymethyl, 1-hydroxyethyl, R10 and R12 are independently selected from the group aminoethyl, N-methylamino, dimethylamino, N-ethylamino, benzylamidocarbonyl, N-(2-chlorobenzyl)amidocarbonyl, methoxycarbonyl, ethoxycarbonyl, amidocarbonyl, Nconsisting of hydrido, amidino, guanidino, carboxy, methylamidocarbonyl, N,N-dimethylamidocarbonyl, Ncrifluoroacetamido, aminomethyl, 1-aminoethyl, 2-2-hydroxyethyl, 2,2,2-trifluoro-1-hydroxyethyl, ethoxy, isopropoxy, propoxy, hydroxy, amino, methoxyamino, ethoxyamino, acetamido,

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phenylethyl)amidocarbonyl, N-benzylamidosulfonyl, N-(2cyclobutylamidocarbonyl, N-cyclopentylamidocarbonyl, Nbenzyloxy, 4-bromo-3-fluorophenoxy, 3-bromobenzyloxy, 4cyclohexylamidocarbonyl, fluoro, chloro, bromo, cyano, trifluoromethycyclohexylmethoxy, cyclopentoxy, benzyl, chlorobenzyl)amidosulfonyl, N-ethylamidocarbonyl, Nylmethylamino, 4-butoxyphenamino, 3-chlorobenzyl, 4isobutylamidocarbonyl, N-(2-butyl)amidocarbonyl, Nbromobenzyloxy, 4-bromobenzylamino, 5-bromopyrid-2chlorophenoxy, 4-chloro-3-ethylphenoxy, 4-chloro-3isopropylamidocarbonyl, N-propylamidocarbonyl, Nethylbenzylamino, 4-chloro-3-ethylphenylamino, 3cyclobutoxy, cyclohexoxy, cyclohexylmethoxy, 4chlorobenzylsulfonyl, 4-chlorophenylamino, 4-N-(3-fluorobenzyl) amidocarbonyl, N-(2trifluoromethylbenzyl) amidocarbonyl, N-(1phenylethyl) amidocarbonyl, N-(1-methyl-1chlorobenzyloxy, 4-chlorobenzyloxy, 4-

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difluorophenoxy, ,5-dimethylphenoxy, 3,4-dimethylphenoxy, difluorobenzyloxy, 4-difluoromethoxybenzyloxy, 2,3-3,4-dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 4cyanopyrid-3-yloxy, 2,3-difluorobenzyloxy, 2,4difluorobenzyloxy, 3,4-difluorobenzyloxy, 2,5difluorobenzyloxy, 3,5-difluorophenoxy, 3,5difluorophenoxy, 2,4-difluorophenoxy, 2,5-

fluorobenzyloxy, 2-fluoro-3-trifluoromethylbenzyloxy, 3methylphenoxy, 4-isopropylbenzyloxy, 3-isopropylphenoxy, isopropylphenoxy, 4-isopropylphenoxy, 4-isopropyl-3fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2ethoxyphenoxy, 4-ethylbenzyloxy, 3-ethylphenoxy, 4fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-4-isopropylphenoxy, 4-isopropyl-3-methylphenoxy, trifluoromethylphenoxy, 4-isopropylbenzyloxy, 3ethylaminophenoxy, 3-ethyl-5-methylphenoxy, 4fluoro-5-trifluoromethylbenzyloxy, 4-fluoro-2trifluoromethylbenzyloxy, 2-fluorophenoxy, 4trifluoromethylbenzyloxy, 4-fluoro-3-

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3-trifluoromethoxyphenoxy, 4-trifluoromethoxyphenoxy, 3trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, trifluoromethylbenzyloxy, 4-trifluoromethylbenzyloxy, phenylethyl, 2-phenylethylamino, phenylsulfonyl, 3phenylamino, 1-phenylethoxy, 2-phenylethoxy, 2-2,4-bis-trifluoromethylbenzyloxy, 3-

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trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, -trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3trifluoromethylthiobenzyloxy, 2,3,4-trifluorophenoxy, 2,3,5-trifluorophenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy) phenoxy, and 3trifluoromethylthiobenzyloxy, 4-

1-Qb-4-Q"-2-R16-3-R17-5-R18-6-R19benzene, 2-Qb-5-Q"-6-R17-4-R18-3-R19pyridine, 3-Qb-6-Q"-2-R16-5-R18-4-R19pyridine, 2-Qb-5-Q"- $3-R^{16}-6-R^{18}$ pyrazine, $3-Q^{b}-6-Q^{s}-2-R^{18}-5-R^{18}-4-R^{19}$ pyridazine, 2-Yo is selected from the group consisting of:

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chlorophenylsulfonyl, 5-chloropyrid-3-yloxy, 2-

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trifluoromethylthiophenoxy;

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time;

group consisting of hydrido, methyl, ethyl, and hydroxy; O' is selected from the group consisting of a bond, R23, R24, and R25 are independently selected from the

CH, and CH,CH,.

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acceptable salt thereof, wherein;

M is N→O;

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sarboxy, amidino, guanidino, methoxy, ethoxy, isopropoxy,

propoxy, hydroxy, amino, aminomethyl, 1-aminoethyl, 2aminoethyl, N-methylamino, dimethylamino, N-ethylamino,

trifluoromethylthio, methylsulfinyl, ethylsulfinyl,

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methylthio, ethylthio, isopropylthio,

methylsulfonyl, ethylsulfonyl, trifluoromethyl,

pentafluoroethyl, 2,2,2-triffluoroethyl, 2,2,3,3,3-

pentafluoropropyl, trifluoromethoxy, 1,1,2,2-

consisting of hydrido, methyl, ethyl, isopropyl, propyl,

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R17 and R18 are independently selected from the group

R19thiazole, and 2-Q-5-Q-4-R17thiazole;

R¹⁶-4-R¹⁷furan, 3-Q⁵-5-Q⁶-4-R¹⁶-2-R¹⁹pyrrole, 2-Q⁵-5-Q⁶-3-R¹⁶-

1-R¹⁷pyrrole, 4-Q^b-2-Q^e-5-R¹⁹imidazole, 2-Q^b-4-Q^e-5-R¹⁷1midazole, 3-Q^b-5-Q^e-4-R¹⁶1soxazole, 5-Q^b-3-Q^e-4-R16180xazole, 2-Q2-5-Q8-4-R16pyrazole, 4-Q2-2-Q8-5-

'n

R¹⁹pyrimidine, 3-Q⁵-5-Q"-4-R¹⁶-2-R¹⁹thiophene, 2-Q⁵-5-Q⁸-3-R16-4-R17thiophene, 3-Qb-5-Q-4-R16-2-R18furan, 2-Qb-5-Q-3-

Q-5-Q-4-R17-6-R18pyrimidine, 5-Q-2-Q-4-R16-6-

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trifluoromethylphenyl, 2-imidazoyl, 2-pyridyl, 3-pyridyl, methoxyaminophenyl, 3-methoxyphenyl, 4-methoxyphenyl, 3dichlorophenyl, 2-fluorophenyl, 3-fluorophenyl, 3,4difluorophenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 3hydroxyphenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-5-chloro-3-trifluoromethyl-2-pyridyl, 4-pyridyl, 2-B is selected from the group consisting of aminophenyl, 3-aminophenyl, 3-amidinophenyl, 4amidinophenyl, 3-carboxyphenyl, 3-carboxy-5methylphenyl, 4-methylphenyl, phenyl, 3-

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thienyl, 3-thienyl, and 3-trifluoromethyl-2-pyridyl; A is selected from the group consisting of CH,

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R16 and R19 are selected from the group consisting of:

cetrafluoroethoxy, fluoro, chloro, bromo, hydroxymethyl,

-hydroxyethyl, 2-hydroxyethyl, and cyano;

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carboxy, amidino, guanidino, methoxy, ethoxy, isopropoxy,

(i) hydrido, methyl, ethyl, isopropyl, propyl,

propoxy, hydroxy, amino, aminomethyl, 1-aminoethyl, 2-

aminoethyl, N-methylamino, dimethylamino, N-ethylamino,

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trifluoromethylthio, methylsulfinyl, ethylsulfinyl,

nethylthio, ethylthio, isopropylthio,

pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3-

pentafluoropropyl, trifluoromethoxy, 1,1,2,2-

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methylsulfonyl, ethylsulfonyl, trifluoromethyl,

Jb is N or C-R1;

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R' and X° are independently selected from the group hydroxyamino, aminomethyl, methylamino, cyano, methyl, trifluoromethyl, methoxy, hydroxymethyl, methoxyamino, methylthio, trifluoromethoxy, fluoro, and chloro; consisting of hydrido, hydroxy, amino, amidino,

Z° is selected from the group consisting of a bond, CH2, O, S, NH, N(CH3), OCH2, and SCH2;

benzylamidocarbonyl)phenyl, 3-amino-5-benzylphenyl, 3-Q is selected from the group consisting of 3amidocarbonyl-5-aminophenyl, 3-amino-5-(N-

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The compound of claim 75 or a pharmaceutically

CH,CH, CF,CH, NHC(O), CH,CH,, and CH2CH,CH2; Ja is Nor C-X';

R2 18 Z0-Q;

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(11) C(NR25)NR21R24 with the proviso that R16, R19, and

tetrafluoroethoxy, fluoro, chloro, bromo, hydroxymethyl,

1-hydroxyethyl, 2-hydroxyethyl, and cyano; and

Qb is C(NR25)NR23R24 or hydrido, with the proviso that

Qb are not simultaneously hydrido;

35

no more than one of R23 and R24 is hydroxy at the same

amino-5-(2-phenylethyl)phenyl, 3-amino-5-

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trifluoromethylbenzyl)amidocarbonyl)phenyl, 3-amino-5-(N-5-(4-trifluoromethylbenzyloxy)phenyl, 3-carboxyphenyl, 3methyl-1-phenylethyl)amidocarbonyl)phenyl, 3-amino-5-(Nbenzylaminophenyl, 3-amino-5-(2-phenylethylamino)phenyl, 3-amino-5-(4-trifluoromethylbenzylamino)phenyl, 3-amino-31aminophenyl, 3-dimethylaminophenyl, 2-fluorophenyl, 3methylphenyl, 5-amino-2-methylthiophenyl, 3-aminophenyl, cyclohexylamidocarbonyl)phenyl, 5-amino-2-fluorophenyl, (1-phenylethyl)amidocarbonyl)phenyl, 3-amino-5-(N-(1carboxy-5-hydroxyphenyl, 3-amino-5-carboxyphenyl, 3chlorobenzy1) amidocarbony1) pheny1, 3-amino-5-(N-(3fluorobenzyl) amidocarbonyl) phenyl, 3-amino-5-(N-(2fluorophenyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 3methoxycarbonylphenyl, 3-amidinophenyl, 3-amino-2chlorophenyl, 2-chlorophenyl, 3-cyanophenyl, 3,5chlorobenzyl)amidosulfonyl)phenyl, 3-amino-5-(Nmethanesulfonylaminophenyl, 2-methoxyphenyl, 3isobutylamidocarbonyl)phenyl, 3-amino-5-(N-(2cyclopentylamidocarbonyl)phenyl, 3-amino-5-(Ncyclobutylamidocarbonyl)phenyl, 3-amino-5-(Nisopropylamidocarbonyl) phenyl, 3-amino-5-(Nbenzylamidosulfonyl)phenyl, 3-amino-5-(N-(2butyl) amidocarbonyl) phenyl, 3-amino-5-(Npropylamidocarbonyl) phenyl, 3-amino-5-(N-3-amino-5-hydroxymethylphenyl, 5-amino-3-3-amino-5-benzyloxyphenyl, 3-amino-5-(2ethylamidocarbonyl)phenyl, 3-amino-5-(Nphenylethoxy) phenyl, 3-amino-5-(N-(2-

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R¹⁹pyridine, 3-Q^b-6-Q^e-2-R¹⁶-5-R¹⁶-4-R¹⁹pyridine,3-Q^b-5-Q^e-4-R16-2-R19thiophene, and 2-Q2-5-Q6-3-R16-4-R17thiophene; 2-Ris-3-R17-5-R18-6-R18benzene, 2-Qb-5-Q8-6-R17-4-R18-3 R^{16} and R^{19} are selected from the group consisting of: methylamino, hydroxy, hydroxymethyl, fluoro, chloro, and (1) hydrido, amidino, amino, aminomethyl, methoxy, cyano; and

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(ii) C(NR23)NR23R24 with the proviso that R16, R19, and Qb are not simultaneously hydrido;

 R^{17} and R^{19} are independently selected from the group consisting of hydrido, fluoro, chloro, hydroxy, hydroxymethyl, amino, carboxy, and cyano; Qb is C(NR25) NR23R24 or hydrido;

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77. The compound of claim 74 having the structure:

R23, R24, and R25 are independently hydrido or methyl;

Q° is CH2.

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substituted by R16, a carbon adjacent to R12 and two atoms from the carbon at the point of attachment is optionally B is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of optionally substituted by R12, the other carbon adjacent or a pharmaceutically acceptable salt thereof, wherein; to the carbon at the point of attachment is optionally attachment of said phenyl or heteroaryl ring to A is

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substituted by R11, a carbon adjacent to R16 and two atoms

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 Y^o is selected from the group consisting of 1-Q^-4-Q"-

trifluoromethylphenyl, 2-trifluoromethylphenyl, 5-amino-

2-thienyl, 5-amino-3-thienyl, 3-bromo-2-thienyl, 3-

pyridyl, 4-pyridyl, 2-thienyl, and 3-thienyl;

S N

methylaminophenyl, 2-methylphenyl, 3-methylphenyl, 4nethylphenyl, phenyl, 3-trifluoroacetamidophenyl, 3-

methoxycarbonylphenyl, 2-methylaminophenyl, 3-

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methoxyphenyl, 3-methoxyaminophenyl, 3-

from the carbon at the point of attachment is optionally substituted by \mathbb{R}^{13} , and any carbon adjacent to both \mathbb{R}^{13} and \mathbb{R}^{13} is optionally substituted by \mathbb{R}^{14} ;

R¹³, R¹³, R¹⁴, and R¹⁶ are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkoxy, hydroxy, amino, alkoxyamino, alkylamino, alkylthio, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, carboalkoxy, carboxy, carboxamido, cyano, and Q²;

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A is a bond or $(CH(R^{15}))_{pa} - (W^7)_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W⁷ is $N(R^7)$;

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R' is hydrido or alkyl;

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 R^{15} is selected from the group consisting of hydrido, halo, alkyl, and haloalkyl,

R¹ and X° are independently selected from the group consisting of hydrido, hydroxy, hydroxyamino, amidino, amino, cyano, hydroxyalkyl, alkoxy, alkyl, alkylthio, aminoalkyl, alkylthio, alkoxyamino, haloalkyl, and halo;

R2 is 20-0;

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Z° is a bond;

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Q is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to 2° is optionally substituted by R³, the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R¹, a carbon adjacent to R³ and two atoms from the carbon at the point of attachment is optionally substituted by R¹, a carbon adjacent to R¹¹ and two atoms from the carbon at the point of attachment is optionally substituted by R¹², and any carbon adjacent to both R¹¹ and R¹² is optionally substituted by R¹²;

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 $R^{9},\ R^{11},\ and\ R^{13}$ are independently selected from the group consisting of hydrido, hydroxy, amino, amidino,

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guanidino, alkylamino, alkylthio, alkoxy, alkylaulfinyl,
alkylsulfonyl, amidosulfonyl, alkyl, halo, haloalkyl,
haloalkoxy, hydroxyalkyl, carboxy, carboxamido, and
cyano;

R¹⁰ and R¹² are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkyl, alkoxy, alkoxyamino, hydroxy, amino, alkylamino, alkylsulfonamido, amidosulfonyl, hydroxyalkyl, aminoalkyl, halo, haloalkyl, carboalkoxy, carboxyamido, carboxyalkyl, and cyano;

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wherein one carbon of said phenyl or said heteroaryl is substituted by Q^{*} , a carbon two or three atoms from the point of attachment of Q^{*} to said phenyl or said heteroaryl is substituted by Q^{*} , a carbon adjacent to the point of attachment of Q^{*} is optionally substituted by R^{1} , another carbon adjacent to the point of attachment of Q^{*} is optionally substituted by R^{1} , a carbon adjacent to Q^{*} is optionally substituted by R^{1} , a carbon adjacent to Q^{*} is optionally substituted by R^{1} , and another carbon adjacent to Q^{*} is optionally substituted by R^{1} , and another carbon adjacent to Q^{*} is optionally substituted by R^{1} ,

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R¹⁷ and R¹⁸ are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano;

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 R^{16} and R^{19} are selected from the group consisting of:

 hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano; and

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(11) $NR^{20}R^{21}$ or $C(NR^{25})NR^{21}R^{24}$, with the proviso that R^{16} , R^{19} , and Q^b are not simultaneously hydrido;

Q^b is selected from the group consisting of NR³⁰R²¹, hydrido, and C(NR²³) NR²³R²¹;

R²⁰, R²¹, R²³, R²⁴, and R²⁵ are independently hydrido or alkyl;

Q" is CH2.

78. The compound of claim 77 or a pharmaceutically acceptable salt thereof, wherein;

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B is selected from the group consisting of phenyl, 2-thienyl, 3-thienyl, 3-thienyl, 3-thienyl, 3-turyl, 2-furyl, 2-pyrrolyl, 3-pyracolyl, 4-imidazolyl, 3-pyrazolyl, 4-imidazolyl, 3-pyrazolyl, 4-imidazolyl, 3-pyrazolyl, 4-thiazolyl, 3-isoxazolyl, and 5-isoxazolyl, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to A is optionally substituted by R²², the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R³⁴, a carbon adjacent to R³⁷ and two atoms from the carbon at the point of attachment is optionally substituted by R³³, a carbon adjacent to R³⁴ and two atoms from the carbon at the point of attachment is optionally substituted by R³⁵, and any carbon adjacent to both R³³ and R³⁵ is optionally substituted by R³⁴.

R¹³, R¹⁴, R¹⁵, and R¹⁶ are independently selected from the group consisting of hydrido, amidino, guanidino, methyl, ethyl, methoxy, ethoxy, hydroxy, amino, N-methylamino, dimethylamino, methoxyamino, methylthio, ethylthio, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, fluoro, chloro, bromo, amidosulfonyl, methylamidosulfonyl, hydroxymethyl, amidocarbonyl, carboxy, cyano, and Q^b;

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A is selected from the group consisting of a bond, NH, N(CH₃), CH₂CH, CH₃CH, and CH₂CH₃;

X° is selected from the group consisting of hydrido, hydroxy, amino, amidino, aminomethyl, cyano, methyl, trifluoromethyl, hydroxymethyl, chloro, and fluoro;

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R¹ is selected from the group consisting of hydrido, hydroxy, hydroxymethyl, amino, aminomethyl, methylamino, cyano, methyl, trifluoromethyl, methoxy, methylthio,

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trifluoromethoxy, fluoro, and chloro;

R² is selected from the group consisting of phemyl, 2-thienyl, 2-puriolyl, 2-imidazolyl, 2-thienyl, 2-thienyl, 2-pyriolyl, and 3-pyriolyl, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to the pyrioline ring is optionally substituted by R², the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R², a carbon adjacent to R³ and two atoms from the carbon at the point of attachment is optionally substituted by R², a carbon adjacent to R³ and two atoms from the carbon at the point of attachment is optionally substituted by R², and any carbon adjacent to both R² and R² and

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R³, R¹¹, and R¹¹ are independently selected from the group consisting of hydrido, methyl, ethyl, methoxy, ethoxy, hydroxy, amino, N-methylamino, N.N-dimethylamino, methylthio, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, fluoro, chloro, bromo, amidosulfonyl, N-methylamidosulfonyl, N-dimethylamidosulfonyl, hydroxymethyl, 1-hydroxyethyl, amidocarbonyl, N-methylamidocarbonyl, N-methylamidocarbonyl, and cyano;

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R¹⁰ and R¹² are independently selected from the group consisting of hydrido, amidino, amidocarbonyl, N-methylamidocarbonyl, N-benzylamidocarbonyl, N-(2-chlorobenzyl) amidocarbonyl, N-(3-

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fluorobenzyl) amidocarbonyl, N-(2trifluoromethylbenzyl) amidocarbonyl, N-(1phenylethyl) amidocarbonyl, N-(1-methyl-1-

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phenylethyl) amidocarbonyl, N-benzylamidosulfonyl, N-chlorobenzyl) amidosulfonyl, N-ethylamidocarbonyl, N-isopropylamidocarbonyl, N-isopropylamidocarbonyl, N-cyclobutylamidocarbonyl, N-cyclobutylamidocarbonyl, N-cyclopentylamidocarbonyl, N-cyclobentylamidocarbonyl, N-cyclobentylamidocarbonyl, N-cyclobentylamidocarbonyl, n-cyclohexylamidocarbonyl, guanidino, methyl, ethyl, methoxy, ethoxy, hydroxymethyl, 1-hydroxyethyl,

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2-hydroxyethyl, carboxy, carboxymethyl, amino, acetamido, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, methanesulfonamido, methoxycarbonyl, fluoro, chloro, methylamidosulfonyl, N,N-dimethylamidosulfonyl, trifluoroacetamido, aminomethyl, N-methylamino, dimethylamino, methoxyamino, amidosulfonyl, Nbromo, and cyano;

3-Qb-5-Q"-4-R16-2-R19furan, 2-Qb-5-Q"-3-R16-4-R17furan, 3-Qb-5-Q-4-R¹⁶-2-R¹⁹pyrrole, 2-Q⁵-5-Q⁴-3-R¹⁶-4-R¹⁷pyrrole, 4-Q⁵-2-Q⁴-1-Qb-4-Q*-2-Rife-3-Ri7-5-Rife-6-Rifbenzene, 2-Qb-5-Q*-6-Ri7-4-R18-3-R18pyridine, 2-Qb-5-Q*-3-R16-4-R17thiophene, 3-Qb-6-Q*-2-R16-5-R18-4-R19pyridine, 3-Qb-5-Q*-4-R16-2-R19thiophene, Y° is selected from the group consisting of: $5-R^{19}$ thiazole, and $2-Q^{5}-5-Q^{4}-4-R^{17}$ thiazole;

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pentafluoroethyl, 2,2,2-trifluoroethyl, trifluoromethoxy, R16, R17, R18, and R19 are independently selected from the group consisting of hydrido, methyl, ethyl, amidino, aminoethyl, 2-aminoethyl, N-methylamino, dimethylamino, guanidino, methoxy, hydroxy, amino, aminomethyl, 1fluoro, chloro, hydroxymethyl, carboxy, and cyano; methylsulfinyl, methylsulfonyl, trifluoromethyl, methylthio, ethylthio, trifluoromethylthio,

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the group consisting of hydrido, methyl, and ethyl; R^{20} , R^{21} , R^{24} , and R^{25} are independently selected Qb is NR20R21 or C(NR25)NR23R24; Q is CH2. from

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79. The compound of claim 78 or a pharmaceutically B is selected from the group consisting of 2acceptable salt thereof, wherein;

methoxyaminophenyl, 3-methoxyphenyl, 4-methoxyphenyl, 3dichlorophenyl, 2-fluorophenyl, 3-fluorophenyl, 3,4difluorophenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 3hydroxyphenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4aminophenyl, 3-aminophenyl, 3-amidinophenyl, 4amidinophenyl, 3-carboxyphenyl, 3-carboxy-5-

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trifluoromethylphenyl, 2-imidazoyl, 2-pyridyl, 3-pyridyl, thienyl, 3-thienyl, and 3-trifluoromethyl-2-pyridyl; 5-chloro-3-trifluoromethyl-2-pyridyl, 4-pyridyl, 2methylphenyl, 4-methylphenyl, phenyl, 3-

X° is selected from the group consisting of hydrido, hydroxy, amino, amidino, aminomethyl, cyano, methyl, trifluoromethyl, hydroxymethyl, and fluoro; A is CH, or CH, CH,

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R1 is selected from the group consisting of hydrido, R2 is selected from the group consisting of 3hydroxy, hydroxymethyl, amino, aminomethyl, cyano, amidocarbonyl-5-aminophenyl, 3-amidocarbonyl-5methyl, trifluoromethyl, and fluoro;

(2-trifluoromethylbenzyl) amidocarbonyl) phenyl, 3-amino-5amino-5-(N-(2-chlorobenzyl)amidocarbonyl)phenyl, 3-amino-5-(N-(3-fluorobenzyl)amidocarbonyl)phenyl, 3-amino-5-(N-(N-(1-phenylethyl)amidocarbonyl)phenyl, 3-amino-5-(N-(1aminophenyl, 3-amino-5-(N-benzylamidocarbonyl)phenyl, 3methyl-1-phenylethyl) amidocarbonyl) phenyl, 3-amino-5-(Nchlorobenzyl)amidosulfonyl)phenyl, 3-amino-5-(Nbenzylamidosulfonyl)phenyl, 3-amino-5-(N-(2-

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cyclohexylamidocarbonyl)phenyl, 5-amino-2-fluorophenyl, cyclopentylamidocarbonyl)phenyl, 3-amino-5-(Nisobutylamidocarbonyl)phenyl, 3-amino-5-(N-(2cyclobutylamidocarbonyl)phenyl, 3-amino-5-(Nbutyl) amidocarbonyl) phenyl, 3-amino-5-(Npropylamidocarbonyl)phenyl, 3-amino-5-(N-

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isopropylamidocarbonyl)phenyl, 3-amino-5-(N-

ethylamidocarbonyl)phenyl, 3-amino-5-(N-

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carboxymethyl-5-hydroxyphenyl, 3-carboxymethylphenyl, 3methylphenyl, 5-amino-2-methylthiophenyl, 3-aminophenyl, 3-carboxyphenyl, 3-carboxy-5-aminophenyl, 3-carboxy-5methoxycarbonylphenyl, 3-amidinophenyl, 3-amino-2chlorophenyl, 2-chlorophenyl, 3-cyanophenyl, 3,5hydroxyphenyl, 3-carboxymethyl-5-aminophenyl, 3-3-amino-5-hydroxymethylphenyl, 5-amino-3-

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trifluoromethylphenyl, 2-trifluoromethylphenyl, 5-aminomethoxyphenyl, 3-methoxyphenyl, 3-methoxyaminophenyl, 3diaminophenyl, 3-dimethylaminophenyl, 2-fluorophenyl, 3methylaminophenyl, 2-methylphenyl, 3-methylphenyl, 4fluorophenyl, 2,5-difluorophenyl, 2-hydroxyphenyl, 3methylphenyl, phenyl, 3-trifluoroacetamidophenyl, 3-2-thienyl, 5-amino-3-thienyl, 3-bromo-2-thienyl, 3hydroxyphenyl, 3-methaneaulfonylaminophenyl, 2methoxycarbonylphenyl, 2-methylaminophenyl, 3pyridyl, 4-pyridyl, 2-thienyl, and 3-thienyl;

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4-R18-3-R19pyridine, 3-Q2-6-Q8-2-R16-5-R18-4-R19pyridine, 3-Q2-1-Qb-4-Q0-2-R16-3-R17-5-R18-6-R18benzene, 2-Qb-5-Q0-6-R17-5-Q*-4-R16-2-R19thiophene, and 2-Q*-5-Q*-3-R16-4-R17thiophene, Yo is selected from the group consisting of:

 R^{16} and R^{19} are independently selected from the group methoxy, methylamino, hydroxy, hydroxymethyl, fluoro, consisting of hydrido, amidino, aminomethyl, chloro, and cyano;

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R17 and R18 are independently selected from the group R23, R24, and R25 are independently hydrido or methyl; consisting of hydrido, fluoro, chloro, hydroxy, hydroxymethyl, amino, carboxy, and cyano; Qb is C (NR23) NR23R24;

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80. The compound of claim 79 or a pharmaceutically acceptable salt thereof, wherein; 25

Q" 18 CH2.

fluorophenyl, 4-methylphenyl, phenyl, 2-imidazoyl, 3chlorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 2pyridyl, 4-pyridyl, and 3-trifluoromethyl-2-pyridyl; B is selected from the group consisting of 3aminophenyl, 3-amidinophenyl, 4-amidinophenyl, 3-

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X° is selected from the group consisting of hydrido, hydroxy, amino, amidino, aminomethyl, cyano, methyl, A 18 CH, or CH, CH2;

trifluoromethyl, hydroxymethyl, and fluoro;

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R¹ is selected from the group consisting of hydrido, 357

hydroxy, hydroxymethyl, amino, aminomethyl, cyano,

methyl, trifluoromethyl, and fluoro;

trifluoromethylbenzyl)amidocarbonyl)phenyl, 3-amino-5-(Nnethy1-1-phenylethyl)amidocarbonyl)phenyl, 3-amino-5-(N-(1-phenylethyl)amidocarbonyl)phenyl, 3-amino-5-(N-(1fluorobenzyl)amidocarbonyl)phenyl, 3-amino-5-(N-(2chlorobenzyl) amidocarbonyl) phenyl, 3-amino-5-(N-(3-R² is selected from the group consisting of 3benzylamidocarbonyl)phenyl, 3-amino-5-(N-(2benzylamidosulfonyl)phenyl, 3-amino-5-(N-(2amidocarbonyl-5-aminophenyl, 3-amino-5-(N-

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chlorobenzyl)amidosulfonyl)phenyl, 3-amino-5-(Nisopropylamidocarbonyl)phenyl, 3-amino-5-(Nethylamidocarbonyl)phenyl, 3-amino-5-(N-

isobutylamidocarbonyl)phenyl, 3-amino-5-(N-(2cyclobutylamidocarbonyl)phenyl, 3-amino-5-(Nbutyl) amidocarbonyl) phenyl, 3-amino-5-(Npropylamidocarbonyl)phenyl, 3-amino-5-(N-

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cyclohexylamidocarbonyl)phenyl, 3-aminophenyl,3-carboxy-5-aminophenyl, 3-chlorophenyl, 3,5-diaminophenyl, 3methanesulfonylaminophenyl, 3-methylaminophenyl, 2cyclopentylamidocarbonyl)phenyl, 3-amino-5-(Ndimethylaminophenyl, 3-hydroxyphenyl, 3-

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trifluoroacetamidophenyl, 3-bromo-2-thienyl, 2-thienyl, methylphenyl, 3-methylphenyl, phenyl, 3and 3-thienyl;

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amidino-2-thienylmethyl, 4-amidinobenzyl, 2-fluoro-4-Yo is selected from the group consisting of 5amidinobenzyl, and 3-fluoro-4-amdinobenzyl.

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The compound of claim 74 having the structure:

 R^2 is 3-aminophenyl, B is phenyl, A is $CH_2,\ Y^0$ is 4or a pharmaceutically acceptable salt thereof, wherein; amidinobenzyl, and R' is chloro; R' is 3-aminophenyl, B is 3-chlorophenyl, A is CH2CH3, Y° is 4-amidinobenzyl, and R¹ is chloro;

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 R^2 is 3-aminophenyl, B is phenyl, A is $CH_2,\ Y^{\circ}$ is 4amidinobenzyl, and R1 is hydrido;

R² is 3-aminophenyl, B is 2-imidazoyl, A is CH₂CH₂, Y° is 4-amidinobenzyl, and R¹ is chloro;

chlorophenyl, A is CH_2CH_2 , Y^{θ} is 4-amidinobenzyl, and R^1 is R2 is 3-amidocarbonyl-5-aminophenyl, B is 3-

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3-chlorophenyl, A is CH2CH3, Y $^{\rm 0}$ is 4-amidinobenzyl, and $\rm R^{\rm 1}$ R' is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is

chlorobenzyl)amidocarbonyl)phenyl, B is 3-chlorophenyl, A is CH2CH2, Y0 is 4-amidinobenzyl, and R1 is chloro; R' is 3-amino-5-(N-(2is chloro;

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chlorobenzyl) amidosulfonyl) phenyl, B is 3-chlorophenyl, A is CH2CH2, Y° is 4-amidinobenzyl, and R¹ is chloro; R2 is 3-amino-5-(N-(2-20

chlorophenyl, A is CH2CH2, Y^0 is 4-amidinobenzyl, and R^1 is trifluoromethylbenzyl)amidocarbonyl) - phenyl, B is 3-R2 is 3-amino-5-(N-(2-

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R2 is 3,5-diaminophenyl, B is 3-chlorophenyl, A is CH,CH,, Yº is 4-amidinobenzyl, and R1 is chloro, R² is 3-amino-5-carboxyphenyl, B is 3-chlorophenyl, A is CH2CH2, Y° is 4-amidinobenzyl, and R¹ is chloro;

chlorophenyl, A is CH_2CH_2 , Y^0 is 4-amidinobenzyl, and R^1 is R' is 3-amidocarbonyl-5-aminophenyl, B is 3hydrido;

3-chlorophenyl, A is CH,CH,, Υ^0 is 4-amidinobenzyl, and R^1 R' is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is

18 hydrido;

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chlorobenzyl) amidocarbonyl) phenyl, B is 3-chlorophenyl, A is CH2CH2, Y° is 4-amidinobenzyl, and R¹ is hydrido; R2 is 3-amino-5-(N-(2-

R2 18 3-amino-5-(N-(2-

chlorobenzyl) amidosulfonyl) phenyl, B is 3-chlorophenyl, A is CH_2CH_2 , Y^{α} is 4-amidinobenzyl, and R^1 is hydrido; 13

R2 is 3-amino-5-(N-(2-

chlorophenyl, A is CH_2CH_2 , Y^0 is 4-amidinobenzyl, and R^1 is trifluoromethylbenzyl)amidocarbonyl) - phenyl, B is 3-

R² is 3,5-diaminophenyl, B is 3-chlorophenyl, A is CH₂CH₂, Y° is 4-amidinobenzyl, and R¹ is hydrido; hydrido;

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R² is 3-amino-5-carboxyphenyl, B is 3-chlorophenyl, A is $\mathrm{CH_2CH_3}$, Y^0 is 4-amidinobenzyl, and R^1 is hydrido.

The compound of claim 67 having the structure: 82.

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or a pharmaceutically acceptable salt thereof, wherein; M is N or N→O; WO 02/42272

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B is selected from the group consisting of hydrido, C2-C8 alkyl, C3-C8 alkyl, C3-C8 alkyl), and C2-C8 haloalkyl, wherein each member of group B is optionally substituted at any carbon up to and including 6 atoms from the point of attachment of B to A with one or more of the group consisting of R²³, R²⁴, R²⁴, and R²⁴;

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R¹³, R¹³, R¹⁵, and R¹⁶ are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkoxy, hydroxy, amino, alkoxyamino, alkylamino, alkylthio, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, hydroxyhaloalkyl, carboalkoxy, carboxamido, cyano, and Q³;

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A is a bond or (CH(R¹¹))_p-(W²)_{rr} wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W² is (R²)NC(O) or N(R²);

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 $\ensuremath{R^{7}}$ is selected from the group consisting of hydrido, hydroxy and alkyl;

R¹⁵ is selected from the group consisting of hydrido halo, alkyl, and haloalkyl;

Jais Nor C-X°;

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Jb is N or C-R1;

R¹ and X° are independently selected from the group consisting of hydrido, hydroxy, hydroxyamino, amidino, amino, cyano, hydroxyalkyl, alkoxy, alkyl, alkylamino, aminoalkyl, alkylthio, alkoxyamino, haloalkyl,

haloalkoxy, and halo;

25

R2 is Z0-Q;

Z° is selected from the group consisting of a bond, CH₂, CH₂CH₂, w°-(CH(R⁴))_p wherein p is 0 or 1 and w° is selected from the group consisting of 0, S, and N(R⁴); R⁴ and R⁴ are independently hydrido or alkyl;

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Q is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to 2° is optionally substituted by R°, the other carbon adjacent to

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the carbon at the point of attachment is optionally substituted by R¹³, a carbon adjacent to R⁹ and two atoms from the carbon at the point of attachment is optionally substituted by R¹⁹, a carbon adjacent to R¹³ and two atoms from the carbon at the point of attachment is optionally substituted by R¹², and any carbon adjacent to both R¹⁹ and R¹² is optionally substituted by R¹¹;

R, R11, and R13 are independently selected from the group consisting of hydrido, hydroxy, amino, amidino, guanidino, alkylamino, alkylthio, alkylsulfonamido, alkylsulfinyl, alkylsulfonyl, amidosulfonyl, alkyl, alkyl, haloalkoxy, hydroxyalkyl, hydroxyhaloalkyl, carboxy, carboxamido, and cyano;

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R¹⁰ and R¹² are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkyl, aryl, aralkyl, cycloalkyl, cycloalkyl, heteroaryl, heterocyclyl, alkoxy, cycloalkylalkoxy, aralkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, heterocyclylalkoxy, hydroxy, amino, alkoxyamino, alkylamino, aralkylamino, heterocyclylamino, heterocyclylamino, heterocyclylamino, heterocyclylamino, heterocyclylamino, arylsulfonnino, alkylsulfonamido, amidosulfonyl, arylsulfinyl, aralkylsulfinyl, aralkylsulfinyl, aralkylsulfonyl, aralkylsulfonyl, aralkylsulfinyl, aralkylsulfonyl,

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 Y^0 is phenyl or a heteroaryl of 5 or 6 ring members, wherein one carbon of said phenyl or said heteroaryl is substituted by Q^{μ} , a carbon two or three atoms from the point of attachment of Q^{μ} to said phenyl or said heteroaryl is substituted by Q^{μ} , a carbon adjacent to the point of attachment of Q^{μ} is optionally substituted by R^{17} , another carbon adjacent to the point of attachment of Q^{μ} is optionally substituted by R^{17} , is optionally substituted by R^{17} , a carbon adjacent to Q^{μ}

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carboxyalkyl, carboxamido, halo, haloalkyl, and cyano;

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cycloalkylsulfonyl, heteroarylsulfonyl, hydroxyalkyl,

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hydroxyhaloalkyl, aminoalkyl, carboalkoxy, carboxy,

is optionally substituted by \mathbb{R}^{16} , and another carbon adjacent to \mathbb{Q}^b is optionally substituted by \mathbb{R}^{19} ,

 R^{17} and R^{18} are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano;

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R16 or R19 are selected from the group consisting of: haloalkylthio, alkoxy, hydroxy, amino, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, (i) hydrido, amidino, guanidino, carboxy,

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(ii) NR20R21, N(R26)C(NR25)N(R23)(R24), and C(NR25)NR23R24, haloalkanoy1, alky1, halo, haloalky1, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano; and

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with the proviso that Ris, Ris, and Qb are not simultaneously hydrido;

hydrido, $C(NR^{25})NR^{23}R^{24}$, and $N(R^{26})C(NR^{25})N(R^{23})$ (R^{24}), with the proviso that no more than one of R^{20} and R^{21} is hydroxy at Q^{b} is selected from the group consisting of $NR^{10}R^{31},$ the same time and with the further proviso that no more than one of R23 and R24 is hydroxy at the same time;

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selected from the group consisting of hydrido, alkyl, and R20, R21, R23, R24, R25, and R26 are independently hydroxy;

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Q* is selected from the group consisting of a bond, CH2, and CH2CH2. 83. The compound of claim 82 or a pharmaceutically acceptable salt thereof, wherein;

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M is N or N-O;

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B is selected from the group consisting of hydrido, ethyl, 2-propynyl,

2-propenyl, propyl, isopropyl, butyl, 2-butenyl, 3butenyl, 2-butynyl, sec-butyl, tert-butyl, isobutyl, 2methylpropenyl, 1-pentyl, 2-pentenyl, 3-pentenyl, 4-

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pentenyl, 2-pentynyl, 3-pentynyl, 2-pentyl, 1-methyl-2pentyl, 1-ethyl-2-propenyl, 2-methylbutyl, 2-methyl-2butenyl, 1-methyl-3-butenyl, 1-methyl-2-butynyl, 3-

methyl-2-pentynyl, 1-methyl-3-pentynyl, 3-hexyl, 1-ethylheptenyl, 5-heptenyl, 6-heptenyl, 2-heptynyl, 3-heptynyl, methyl-3-hexenyl, 1-methyl-4-hexenyl, 1-methyl-5-hexenyl, 4-heptynyl, 5-heptynyl, 2-heptyl, 1-methyl-2-hexenyl, 1methylbutyl, 3-methyl-2-butenyl, 3-methyl-3-butenyl, 1ethyl-2-butynyl, 1-heptyl, 2-heptenyl, 3-heptenyl, 4pentenyl, 1-methyl-3-pentenyl, 1-methyl-4-pentenyl, 1hexyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 5-hexenyl, 2-2-butenyl, 1-ethyl-3-butenyl, 1-propyl-2-propenyl, 1butenyl, 2-methyl-3-butenyl, 2-methyl-3-butynyl, 3hexynyl, 3-hexynyl, 4-hexynyl, 2-hexyl, 1-methyl-2-1-methyl-2-hexynyl, 1-methyl-3-hexynyl, 1-methyl-4hexynyl, 3-heptyl, 1-ethyl-2-pentenyl, 1-ethyl-3-

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trifluoroethyl, 2,2-difluoropropyl, 4-trifluoromethylpentenyl, 1-ethyl-4-pentenyl, 1-butyl-2-propenyl, 1ethyl-2-pentynyl, 1-ethyl-3-pentynyl, 2,2,2-

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wherein each member of group B is optionally substituted at any carbon up to and including 5 atoms from the point 5,5,6,6,6-pentafluorohexyl, and 3,3,3-trifluoropropyl, of attachment of B to A with one or more of the group 5,5,5-trifluoropentyl, 4-trifluoromethylpentyl, consisting of R12, R13, R14, R15, and R16;

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guanidino R12, R13, R14, R15, and R16 are independently selected carboxy, methoxy, ethoxy, isopropoxy, propoxy, hydroxy, from the group consisting of hydrido, amidino, amino, methoxyamino, ethoxyamino, acetamido,

trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, tetrafluoroethoxy, fluoro, chloro, bromo, amidosulfonyl, 2,2,3,3,3-pentafluoropropyl, trifluoromethoxy, 1,1,2,2hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 2,2,2trifluoroacetamido, N-methylamino, dimethylamino, Nethylamino, methylthio, ethylthio, isopropylthio, N-methylamidosulfonyl, N,N-dimethylamidosulfonyl,

ethoxycarbonyl, amidocarbonyl, N-methylamidocarbonyl, trifluoro-1-hydroxyethyl, methoxycarbonyl N, N-dimethylamidocarbonyl, cyano, and Qb; A is selected from the group consisting of bond, NH, N(CH₃), N(OH), CH₂, CH₃CH, CF₃CH, NHC(O), N(CH₃)C(O), C(O)NH, C(O)N(CH3), CH2CH3, CH3CH2CH2, and CF, CHCH2;

Ja is N or C-X°;

Jb is N or C-R1;

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R' and X' are independently selected from the group methoxyamino, methylthio, ethylthio, trifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, chloro, and bromo; dimethylamino, cyano, methyl, ethyl, trifluoromethyl, hydroxyamino, aminomethyl, 1-aminoethyl, methylamino, pentafluoroethyl, 2,2,2-trifluoroethyl, methoxy, consisting of hydrido, hydroxy, amino, amidino, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, R2 19 20-0;

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Z° is selected from the group consisting of a bond, CH2, CH2CH2, O, S, NH, N(CH3), OCH2, SCH2, N(H)CH2, and

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carbon adjacent to R13 and two atoms from the carbon at the adjacent to the carbon at the point of attachment of said carbon adjacent to R' and two atoms from the carbon at the phenyl or heteroaryl ring to Z° is optionally substituted pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, point of attachment is optionally substituted by \mathbb{R}^{12} , and 4-pyridazinyl, and 1,3,5-triazin-2-yl, wherein a carbon point of attachment is optionally substituted by \mathbb{R}^{10} , a point of attachment is optionally substituted by R13, a Q is selected from the group consisting of phenyl, 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3pyrazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 2pyrroly1, 2-imidazoly1, 4-imidazoly1, 3-pyrazoly1, 4by R3, the other carbon adjacent to the carbon at the pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-

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any carbon adjacent to both R¹º and R¹² is optionally substituted by R11;

R, R11, and R13 are independently selected from the

group consisting of hydrido, amidino, guanidino, carboxy, isopropoxy, propoxy, hydroxy, amino, N-methylamino, N,Nisopropylthio, trifluoromethyl, pentafluoroethyl, 2,2,2dimethylamino, N-ethylamino, methylthio, ethylthio, methyl, ethyl, propyl, isopropyl, methoxy, ethoxy, trifluoroethyl, 2,2,3,3,3-pentafluoropropyl,

hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 2,2,2chloro, bromo, methanesulfonamido, amidosulfonyl, Ntrifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, methylamidocarbonyl, N,N-dimethylamidocarbonyl, and methylamidosulfonyl, N,N-dimethylamidosulfonyl, trifluoro-1-hydroxyethyl, amidocarbonyl, N-

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carboxymethyl, methyl, ethyl, propyl, isopropyl, methoxy, R10 and R13 are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy ethoxy, isopropoxy, propoxy, hydroxy, amino, cyano;

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methanesulfonamido, amidosulfonyl, N-methylamidosulfonyl, aminoethyl, N-methylamino, dimethylamino, N-ethylamino, trifluoroacetamido, aminomethyl, 1-aminoethyl, 2methoxyamino, ethoxyamino, acetamido,

N, N-dimethylamidosulfonyl, hydroxymethyl, 1-hydroxyethyl, methoxycarbonyl, ethoxycarbonyl, amidocarbonyl, N-2-hydroxyethyl, 2,2,2-trifluoro-1-hydroxyethyl,

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benzylamidocarbonyl, N-(2-chlorobenzyl)amidocarbonyl, Nmethylamidocarbonyl, N,N-dimethylamidocarbonyl, N-(3-fluorobenzyl) amidocarbonyl, N-(2-

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phenylethyl) amidocarbonyl, N-benzylamidosulfonyl, N-(2trifluoromethylbenzyl) amidocarbonyl, N-(1phenylethyl) amidocarbonyl, N-(1-methyl-1-

chlorobenzyl) amidosulfonyl, N-ethylamidocarbonyl, Nisobutylamidocarbonyl, N-(2-butyl)amidocarbonyl, Nisopropylamidocarbonyl, N-propylamidocarbonyl, N-

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trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy,

trifluoromethylbenzyloxy, 4-trifluoromethylbenzyloxy,

2,4-bis-trifluoromethylbenzyloxy, 3-

dimethylbenzyloxy, 4-ethoxyphenoxy, 4-ethylbenzyloxy, 3-N-cyclopentylamidocarbonyl, Nbenzyloxy, 4-bromo-3-fluorophenoxy, 3-bromobenzyloxy, 4cyclohexylamidocarbonyl, fluoro, chloro, bromo, cyano, trifluoromethycyclohexylmethoxy, cyclopentoxy, benzyl, ylmethylamino, 4-butoxyphenamino, 3-chlorobenzyl, 4difluorobenzyloxy, 4-difluoromethoxybenzyloxy, 2,3bromobenzyloxy, 4-bromobenzylamino, 5-bromopyrid-2chlorophenoxy, 4-chloro-3-ethylphenoxy, 4-chloro-3ethylbenzylamino, 4-chloro-3-ethylphenylamino, 3cyanopyrid-3-yloxy, 2,3-difluorobenzyloxy, 2,4cyclobutoxy, cyclohexoxy, cyclohexylmethoxy, 4chlorophenylsulfonyl, 5-chloropyrid-3-yloxy, 2difluorobenzyloxy, 3,4-difluorobenzyloxy, 2,5chlorobenzylsulfonyl, 4-chlorophenylamino, 4methylphenoxy, 4-fluorobenzyloxy, 2-fluoro-3ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5difluorobenzyloxy, 3,5-difluorophenoxy, 3,5dimethylphenoxy, 3,4-dimethylbenzyloxy, 3,5difluorophenoxy, 2,4-difluorophenoxy, 2,5difluorophenoxy, 3,5-dimethylphenoxy, 3,4chlorobenzyloxy, 4-chlorobenzyloxy, 4trifluoromethylbenzyloxy, 3-fluoro-5cyclobutylamidocarbonyl,

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4-R18-3-R19pyridine, 3-Qb-6-Q8-2-R16-5-R18-4-R19pyridine, 2-Qb-Q-3-R16-4-R17thiophene, 3-Q-5-Q-4-R16-2-R19furan, 2-Q-5-Q-1-Qb-4-Q"-2-R16-3-R17-5-R18-6-R19benzene, 2-Qb-5-Q"-6-R17- R^{17} and R^{10} are independently selected from the group carboxy, amidino, guanidino, methoxy, ethoxy, isopropoxy, R19pyridazine, 2-Qb-5-Q0-4-R17-6-R18pyrimidine, 5-Qb-2-Q0-4-R¹⁶-6-R¹⁹pyrimidine, 3-Q^b-5-Q^e-4-R¹⁶-2-R¹⁹thiophene, 2-Q^b-5consisting of hydrido, methyl, ethyl, isopropyl, propyl, tetrafluoroethoxy, fluoro, chloro, bromo, hydroxymethyl, 3-R16-4-R17furan, 3-Qb-5-Q-4-R16-2-R19pyrrole, 2-Qb-5-Q-3aminoethyl, N-methylamino, dimethylamino, N-ethylamino, propoxy, hydroxy, amino, aminomethyl, 1-aminoethyl, 2-4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-2,3,5-trifluorophenoxy, 3-pentafluoroethylphenoxy, 3trifluoromethylthiobenzyloxy, 2,3,4-trifluorophenoxy, R16-4-R17pyrrole, 4-Qb-2-Q"-5-R191midazole, 2-Qb-4-Q"-5trifluoromethylthio, methylsulfinyl, ethylsulfinyl, pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3-R¹⁷1midazole, 3-Q⁵-5-Q⁸-4-R¹⁶1Boxazole, 5-Q⁵-3-Q⁸-4-Yo is selected from the group consisting of: R'ssoxazole, 2-Qb-5-Q"-4-R'spyrazole, 4-Qb-2-Q"-5methylsulfonyl, ethylsulfonyl, trifluoromethyl, 5-Q"-3-R16-6-R18pyrazine, 3-Qb-6-Q"-2-R18-5-R18-4pentafluoropropyl, trifluoromethoxy, 1,1,2,2-1-hydroxyethyl, 2-hydroxyethyl, and cyano; (1,1,2,2-tetrafluoroethoxy)phenoxy, and 3-R'thiazole, and 2-Q'-5-Q'-4-R'Thiazole; methylthio, ethylthio, isopropylthio, trifluoromethylthiobenzyloxy, 4trifluoromethylthiophenoxy; 20 30 2 15 25

carboxy, amidino, guanidino, methoxy, ethoxy, isopropoxy

(i) hydrido, methyl, ethyl, isopropyl, propyl,

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3-trifluoromethoxyphenoxy, 4-trifluoromethoxyphenoxy, 3-

trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy,

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phenylethyl, 2-phenylethylamino, phenylsulfonyl, 3-

methylphenoxy, 4-isopropylbenzyloxy, 3-isopropylphenoxy,

4-isopropylphenoxy, 4-isopropyl-3-methylphenoxy, phenylamino, 1-phenylethoxy, 2-phenylethoxy, 2-

isopropylphenoxy, 4-isopropylphenoxy, 4-isopropyl-3-

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fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-

trifluoromethylbenzyloxy, 2-fluorophenoxy, 4-

trifluoromethylbenzyloxy, 4-fluoro-2trifluoromethylbenzyloxy, 4-fluoro-3-

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fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-

trifluoromethylphenoxy, 4-isopropylbenzyloxy, 3-

R16 or R19 are selected from the group consisting of:

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propoxy, hydroxy, amino, aminomethyl, 1-aminoethyl, 2aminoethyl, N-methylamino, dimethylamino, N-ethylamino, methylthio, ethylthio, isopropylthio, trifluoromethylthio, methylsulfinyl, ethylsulfinyl, methylsulfonyl, ethylsulfonyl, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3pentafluoropropyl, trifluoromethoxy, 1,1,2,2tetrafluoroethoxy, fluoro, chloro, bromo, hydroxymethyl,

1-hydroxyethyl, 2-hydroxyethyl, and cyano; and (11) NR²⁰R²¹, C(NR²³)NR²³R²⁴, and N(R²⁶)C(NR²³)N(R²³)(R²⁴), with the proviso that R¹⁶, R¹⁹, and Q^b are not simultaneously hydrido;

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 Q^b is selected from the group consisting of $NR^{20}R^{21}$, hydrido, $C(NR^{21})NR^{21}R^{24}$, and $N(R^{24})C(NR^{21})N(R^{21})$ (R^{24}), with the proviso that no more than one of R^{20} and R^{21} is hydroxy at the same time and with the further proviso that no more than one of R^{21} and R^{24} is hydroxy at the same time;

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R²⁰, R²¹, R²¹, R²¹, and R²¹ are independently selected from the group consisting of hydrido, methyl, ethyl, propyl, butyl, isopropyl, and hydroxy;

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Q' 18 selected from the group consisting of a bond, CH₂, and CH₂CH₃.

84. The compound of claim 83 or a pharmaceutically acceptable salt thereof, wherein;

M is N→O;

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B is selected from the group consisting of hydrido, ethyl, 2-propenyl,

2-propynyl, propyl, isopropyl, butyl, 2-butyl, (R)-2-butyl, (S)-2-butyl, tert-butyl, isobutyl, 1-pentyl, 3-pentyl, 2-methylbutyl, 2,2,2-trifluoroethyl, 6-amidocarbonylhexyl, 4-methyl-2-pentyl, 3-hydroxypropyl, 1-methoxy-2-propyl, 2-methoxyethyl, 2-methyl-2-butyl, 3-methyl-2-butyl, 2-dimethylaminopropyl, 2-cyanoethyl, 6-hydroxyhexyl, 2-hydroxyethyl, 2-amidinoethyl, 2-guanidinoethyl, 3-guanidinopropyl, 4-guanidinobutyl, 3-

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hydroxypropyl, 4-hydroxybutyl, 6-cyanohexyl, 2-dimethylaminoethyl, 3-methylbutyl, 2-methylbutyl, (8)-2-methylbutyl, 3-aminopropyl, 2-hexyl, and 4-aminobutyl;

A is selected from the group consisting of a bond, CH, NHC(0), CH,CH, CH,CH,CH, and CH,CHCH,;

Ja is Nor C-X';

Jb is N or C-R1;

R¹ and X° are independently selected from the group consisting of hydroxy, amino, amidino, hydroxyamino, aminomethyl, methylamino, cyano, methyl, trifluoromethyl, methoxy, hydroxymethyl, methoxyamino, methylthio, trifluoromethoxy, fluoro, and chloro, R² is 2°-Q;

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 Z° is selected from the group consisting of a bond, CH_{2} , O, S, NH, N(CH,), OCH,, and SCH,;

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Q is selected from the group consisting of 3-amidocarbonyl-5-aminophenyl, 3-amino-5-(N-benzylamidocarbonyl)phenyl, 3-amino-5-benzylphenyl, 3-amino-5-(2-phenylethyl)phenyl, 3-amino-5-

benzylaminophenyl, 3-amino-5-(2-phenylethylamino)phenyl,
3-amino-5-benzyloxyphenyl, 3-amino-5-(2phenylethoxy)phenyl, 3-amino-5-(N-(2chlorobenzyl)amidocarbonyl)phenyl, 3-amino-5-(N-(3-

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fluorobenzyl)amidocarbonyl)phenyl, 3-amino-5-(N-(2trifluoromethylbenzyl)amidocarbonyl)phenyl, 3-amino-5-(N(1-phenylethyl)amidocarbonyl)phenyl, 3-amino-5-(N-(1-

(1-phenylethyl) amidocarbonyl) phenyl, 3-amino-5-(N-(1methyl-1-phenylethyl) amidocarbonyl) phenyl, 3-amino-5-(Nbenzylamidosulfonyl) phenyl, 3-amino-5-(N-(2chlorobenzyl) amidosulfonyl) phenyl, 3-amino-5-(N-

ethylamidocarbonyl)phenyl, 3-amino-5-(N-isopropylamidocarbonyl)phenyl, 3-amino-5-(N-propylamidocarbonyl)phenyl, 3-amino-5-(N-isobutylamidocarbonyl)phenyl, 3-amino-5-(N-butyl)amidocarbonyl)phenyl, 3-amino-5-(N-cabutyl)amidocarbonyl)phenyl, 3-amino-5-(N-cabutyl)amidocarbonyl)

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cyclobutylamidocarbonyl)phenyl, 3-amino-5-(N-cyclopentylamidocarbonyl)phenyl, 3-amino-5-(N-

cyclohexylamidocarbonyl)phenyl, 5-amino-2-fluorophenyl,

3-amino-5-hydroxymethylphenyl, 5-amino-3-

methoxycarbonylphenyl, 3-amidinophenyl, 3-amino-2-

methylphenyl, 5-amino-2-methylthiophenyl, 3-aminophenyl,

3-amino-5-(4-trifluoromethylbenzylamino)phenyl, 3-amino-

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5-(4-trifluoromethylbenzyloxy)phenyl, 3-carboxyphenyl, 3carboxy-5-hydroxyphenyl, 3-amino-5-carboxyphenyl, 3-

chlorophenyl, 2-chlorophenyl, 3-cyanophenyl, 3,5-

diaminophenyl, 3-dimethylaminophenyl, 2-fluorophenyl, 3-

fluorophenyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 3-10

nethanesulfonylaminophenyl, 2-methoxyphenyl, 3-

methoxyphenyl, 3-methoxyaminophenyl, 3-

methoxycarbonylphenyl, 2-methylaminophenyl, 3-

methylaminophenyl, 2-methylphenyl, 3-methylphenyl, 4methylphenyl, phenyl, 3-trifluoroacetamidophenyl, 3-

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trifluoromethylphenyl, 2-trifluoromethylphenyl, 5-amino-2-thienyl, 5-amino-3-thienyl, 3-bromo-2-thienyl, 3pyridyl, 4-pyridyl, 2-thienyl, and 3-thienyl;

Yo is selected from the group consisting of:

1-Qb-4-Qs-2-Rt6-3-Rt7-5-Rt8-6-Rt9benzene, 2-Qb-5-Qs-6-Rt7-4-R18-3-R19pyridine, 3-Qb-6-Q"-2-R16-5-R18-4-R19pyridine, 3-Qb-

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5-Q*-4-R16-2-R19thiophene, and 2-Q*-5-Q*-3-R16-4-R17thiophene, R16 and R19 are selected from the group consisting of:

methylamino, hydroxy, hydroxymethyl, fluoro, chloro, and (i) hydrido, amidino, amino, aminomethyl, methoxy,

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Q are not simultaneously hydrido and not more than one of (ii) C(NR23)NR33R24 with the proviso that R16, R19, and

 R^{17} and R^{18} are independently selected from the group R16 may (C(NR25)NR23 R24 at the same time;

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consisting of hydrido, fluoro, chloro, hydroxy, hydroxymethyl, amino, carboxy, and cyano;

R23, R24, and R25 are independently hydrido or methyl; Qb is C(NR25) NR23R24 or hydrido; Q" is CH2.

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The compound of claim 82 having the structure: 85.

B is selected from the group consisting of hydrido or a pharmaceutically acceptable salt thereof, wherein;

from the point of attachment of B to A with one or more haloalkyl, wherein each member of group B is optionally substituted at any carbon up to and including 6 atoms C2-C8 alkyl, C3-C8 alkenyl, C3-C8 alkynyl, and C2-C8 of the group consisting of R12, R13, R14, R15, and R16;

hydroxyalkyl, carboalkoxy, carboxy, carboxamido, cyano, haloacetamido, amidino, guanidino, alkoxy, hydroxy, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy, from the group consisting of hydrido, acetamido, amino, alkoxyamino, alkylamino, alkylthio,

R12, R11, R14, R15, and R16 are independently selected

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A is a bond or $(CH(R^{15}))_{pa}$ - $(W^7)_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W' is

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R' is hydrido or alkyl;

R15 is selected from the group consisting of hydrido, halo, alkyl, and haloalkyl; 20

R' and X° are independently selected from the group consisting of hydrido, hydroxy, hydroxyamino, amidino, amino, cyano, hydroxyalkyl, alkoxy, alkyl, alkylamino,

aminoalkyl, alkylthio, alkoxyamino, haloalkyl, haloalkoxy, and halo;

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R2 is Z0-Q;

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Zo is a bond;

optionally substituted by R', the other carbon adjacent to substituted by R¹², and any carbon adjacent to both R¹⁰ and substituted by R10, a carbon adjacent to R13 and two atoms from the carbon at the point of attachment is optionally from the carbon at the point of attachment is optionally substituted by R13, a carbon adjacent to R9 and two atoms Q is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to 2° is the carbon at the point of attachment is optionally R12 is optionally substituted by R11;

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R, R11, and R13 are independently selected from the guanidino, alkylamino, alkylthio, alkoxy, alkyleulfinyl, alkylsulfonyl, amidosulfonyl, alkyl, halo, haloalkyl, group consisting of hydrido, hydroxy, amino, amidino, haloalkoxy, hydroxyalkyl, carboxy, carboxamido, and

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 R^{10} and R^{12} are independently selected from the group cyano;

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amidino, guanidino, alkyl, alkoxy, alkoxyamino, hydroxy, hydroxyalkyl, aminoalkyl, halo, haloalkyl, carboalkoxy, amino, alkylamino, alkylsulfonamido, amidosulfonyl consisting of hydrido, acetamido, haloacetamido, carboxy, carboxamido, carboxyalkyl, and cyano;

point of attachment of Q $^{\circ}$ is optionally substituted by R 17 heteroaryl is substituted by Q^b, a carbon adjacent to the Yo is phenyl or a heteroaryl of 5 or 6 ring members, substituted by Q°, a carbon two or three atoms from the another carbon adjacent to the point of attachment of Q° wherein one carbon of said phenyl or said heteroaryl is is optionally substituted by R18, a carbon adjacent to is optionally substituted by R16, and another carbon point of attachment of Q" to said phenyl or said adjacent to Qb is optionally substituted by R19;

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 \mathbb{R}^{17} and \mathbb{R}^{18} are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy,

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alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano;

 R^{16} and R^{19} are selected from the group consisting of:

alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, (1) hydrido, amidino, guanidino, carboxy,

(11) NR20R21, N(R26)C(NR25)N(R21)(R24), and C(NR23)NR23R34, hydroxyalkyl, aminoalkyl, and cyano; and

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with the proviso that R16, R19, and Qb are not simultaneously hydrido;

R20, R21, R21, R24, R25, and R26 are independently hydrido Qb is selected from the group consisting of NR20R21, hydrido, N(R15)C(NR15)N(R10) (R24), and C(NR25)NR13R24;

o is CH2.

or alkyl;

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86. The compound of claim 85 or a pharmaceutically

acceptable salt thereof, wherein;

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2-butenyl, 2-butynyl, sec-butyl, tert-butyl, isobutyl, 2-3-heptynyl, 4-heptynyl, 5-heptynyl, 2-heptyl, 1-methyl-2-2-methyl-2-butenyl, 3-methylbutyl, 3-methyl-2-butenyl, 1heptenyl, 3-heptenyl, 4-heptenyl, 5-heptenyl, 2-heptynyl, B is selected from the group consisting of hydrido, ethyl, 2-propenyl, 2-propynyl, propyl, isopropyl, butyl, pentynyl, 3-pentynyl, 2-pentyl, 3-pentyl, 2-methylbutyl, hexyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 2-hexynyl, 3methylpropenyl, 1-pentyl, 2-pentenyl, 3-pentenyl, 2hexynyl, 4-hexynyl, 2-hexyl, 1-methyl-2-pentenyl, 1hexenyl, 1-methyl-3-hexenyl, 1-methyl-4-hexenyl, 1methyl-3-pentenyl, 1-methyl-2-pentynyl, 1-methyl-3pentynyl, 3-hexyl, 1-ethyl-2-butenyl, 1-heptyl, 2-

methyl-2-hexynyl, 1-methyl-3-hexynyl, 1-methyl-4-hexynyl, 3-heptyl, 1-ethyl-2-pentenyl, 1-ethyl-3-pentenyl, 1-

wherein each member of group B is optionally substituted at any carbon up to and including 5 atoms from the point trifluoroethyl, 2,2-difluoropropyl, 4-trifluoromethyl-5,5,6,6,6-pentafluorohexyl, and 3,3,3-trifluoropropyl, of attachment of B to A with one or more of the group 5,5,5-trifluoropentyl, 4-trifluoromethylpentyl, ethyl-2-pentynyl, 1-ethyl-3-pentynyl, 2,2,2consisting of R12, R11, R14, R15, and R16;

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from the group consisting of hydrido, amidino, guanidino, trifluoroethyl, fluoro, chloro, bromo, amidosulfonyl, N- R^{12} , R^{13} , R^{14} , R^{15} , and R^{16} are independently selected methylamino, dimethylamino, methoxyamino, methylthio, ethylthio, trifluoromethyl, pentafluoroethyl, 2,2,2methyl, ethyl, methoxy, ethoxy, hydroxy, amino, Nmethylamidosulfonyl, hydroxymethyl, amidocarbonyl,

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A is selected from the group consisting of: carboxy, cyano, and Qb;

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(i) a bond, NH, N(CH3), CH2, CH3CH, and CH2CH3; and

CH,CH,N(CH,CH,) with the proviso that B is hydrido; (ii) CH₂N(CH₃), CH₂N(CH₂CH₃), CH₂CH₂N(CH₃), and

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X° is selected from the group consisting of hydrido, hydroxy, amino, amidino, aminomethyl, cyano, methyl, trifluoromethyl, hydroxymethyl, chloro, and fluoro;

 \mathbb{R}^1 is selected from the group consisting of hydrido, hydroxy, hydroxymethyl, amino, aminomethyl, methylamino, cyano, methyl, trifluoromethyl, methoxy, methylthio, trifluoromethoxy, fluoro, and chloro;

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sarbon adjacent to the carbon at the point of attachment is optionally substituted by \mathbb{R}^{13} , a carbon adjacent to \mathbb{R}^9 and two atoms from the carbon at the point of attachment pyridine ring is optionally substituted by R', the other wherein a carbon adjacent to the carbon at the point of R' is selected from the group consisting of phenyl, attachment of said phenyl or heteroaryl ring to the thiazolyl, 3-isoxazolyl, 2-pyridyl, and 3-pyridyl, 2-thienyl, 2-furyl, 2-pyrrolyl, 2-imidazolyl, 2-

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is optionally substituted by R¹⁰, a carbon adjacent to R¹³ is optionally substituted by R12, and any carbon adjacent and two atoms from the carbon at the point of attachment to both R10 and R12 is optionally substituted by R11;

ethoxy, hydroxy, amino, N-methylamino, N,N-dimethylamino, trifluoroethyl, fluoro, chloro, bromo, amidosulfonyl, N-R, R11, and R13 are independently selected from the methylthio, trifluoromethyl, pentafluoroethyl, 2,2,2group consisting of hydrido, methyl, ethyl, methoxy, hydroxymethyl, 1-hydroxyethyl, amidocarbonyl, Nmethylamidosulfonyl, N,N-dimethylamidosulfonyl, methylamidocarbonyl, carboxy, and cyano;

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R10 and R12 are independently selected from the group consisting of hydrido, amidino, amidocarbonyl, Nmethylamidocarbonyl, N-benzylamidocarbonyl, N-(2-N- (3chlorobenzyl) amidocarbonyl,

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fluorobenzyl) amidocarbonyl, N-(2-

trifluoromethylbenzyl)amidocarbonyl, N-(1phenylethyl) amidocarbonyl, N-(1-methyl-1-

N- (2chlorobenzyl)amidosulfonyl, N-ethylamidocarbonyl, Nisobutylamidocarbonyl, N-(2-butyl)amidocarbonyl, Nphenylethyl amidocarbonyl, N-benzylamidosulfonyl, isopropylamidocarbonyl, N-propylamidocarbonyl, N-

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2-hydroxyethyl, carboxy, carboxymethyl, amino, acetamido, cyclobutylamidocarbonyl, N-cyclopentylamidocarbonyl, Nmethoxy, ethoxy, hydroxy, hydroxymethyl, 1-hydroxyethyl, cyclohexylamidocarbonyl, guanidino, methyl, ethyl,

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trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, methanesulfonamido, methoxycarbonyl, fluoro, chloro, trifluoroacetamido, aminomethyl, N-methylamino, methylamidosulfonyl, N,N-dimethylamidosulfonyl, dimethylamino, methoxyamino, amidosulfonyl, N-

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1-Qb-4-Qf-2-R16-3-R17-5-R18-6-R19benzene, 2-Qb-5-Q'-6-R17-4-R18-3-R19pyridine, 2-Qb-5-Qe-3-R16-4-R17thiophene, 3-Qb-6-Yo is selected from the group consisting of:

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bromo, and cyano;

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Q*-4-R16-2-R19pyrrole, 2-Qb-5-Q*-3-R16-4-R17pyrrole, 4-Qb-2-Q*-3-Qb-5-Q-4-R16-2-R19furan, 2-Qb-5-Q-3-R16-4-R17furan, 3-Qb-5-Q"-2-R16.5-R18-4-R19pyridine, 3-Qb-5-Q"-4-R16-2-R19thiophene, 5-R19thiazole, and 2-Qb-5-Q-4-R17thiazole;

pentafluoroethyl, 2,2,2-trifluoroethyl, trifluoromethoxy, R¹⁶, R¹⁷, R¹⁸, and R¹⁹ are independently selected from the group consisting of hydrido, methyl, ethyl, amidino, aminoethyl, 2-aminoethyl, N-methylamino, dimethylamino, guanidino, methoxy, hydroxy, amino, aminomethyl, 1fluoro, chloro, hydroxymethyl, carboxy, and cyano; methylsulfinyl, methylsulfonyl, trifluoromethyl, methylthio, ethylthio, trifluoromethylthio,

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 Q^{\flat} is selected from the group consisting of $NR^{20}R^{23},$ C(NR25) NR22R24, and N(R26) C(NR25) N(R23) (R24);

selected from the group consisting of hydrido, methyl, $R^{20},\ R^{21},\ R^{23},\ R^{24},\ R^{25},\ and\ R^{26}\,are\ independently$ and ethyl;

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o is CH2.

87. The compound of claim 86 or a pharmaceutically acceptable salt thereof, wherein;

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-amidocarbonylhexyl, 4-methyl-2-pentyl, 3-hydroxypropyl, -methoxy-2-propy1, 2-methoxyethy1, 2-methy1-2-buty1, 3dimethylaminoethyl, 3-methylbutyl, 2-methylbutyl, (S)-2-2-buty1, (R)-2-buty1, (S)-2-buty1, tert-buty1, isobuty1, ethyl, 2-propenyl, 2-propynyl, propyl, isopropyl, butyl, -pentyl, 3-pentyl, 2-methylbutyl, 2,2,2-trifluoroethyl, B is selected from the group consisting of hydrido, methyl-2-butyl, 2-dimethylaminopropyl, 2-cyanoethyl, 6guanidinoethyl, 3-guanidinopropyl, 4-guanidinobutyl, 3methylbutyl, 3-aminopropyl, 2-hexyl, and 4-aminobutyl; ydroxyhexyl, 2-hydroxyethyl, 2-amidinoethyl, 2nydroxypropyl, 4-hydroxybutyl, 6-cyanohexyl, 2-

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X° is selected from the group consisting of hydrido, CH2, CH3CH, and CH2CH1;

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A is selected from the group consisting of a bond,

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hydroxy, amino, amidino, aminomethyl, cyano, methyl, trifluoromethyl, hydroxymethyl, and fluoro; R1 is selected from the group consisting of hydrido, hydroxy, hydroxymethyl, amino, aminomethyl, cyano, methyl, trifluoromethyl, and fluoro;

amino-5-(N-(2-chlorobenzyl)amidocarbonyl)phenyl, 3-amino-(2-trifluoromethylbenzyl)amidocarbonyl)phenyl, 3-amino-5-5-(N-(3-fluorobenzyl)amidocarbonyl)phenyl, 3-amino-5-(Naminophenyl, 3-amino-5-(N-benzylamidocarbonyl)phenyl, 3-(N-(1-phenylethyl)amidocarbonyl)phenyl, 3-amino-5-(N-(1methyl-1-phenylethyl)amidocarbonyl)phenyl, 3-amino-5-(Nis selected from the group consisting of 3amidocarbonyl-5-aminophenyl, 3-amidocarbonyl-5benzylamidosulfonyl)phenyl, 3-amino-5-(N-(2-

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chlorobenzyl) amidosulfonyl) phenyl, 3-amino-5-(Nisobutylamidocarbonyl)phenyl, 3-amino-5-(N-(2lsopropylamidocarbonyl) phenyl, 3-amino-5-(Npropylamidocarbonyl) phenyl, 3-amino-5-(Nethylamidocarbonyl)phenyl, 3-amino-5-(N-

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cyclohexylamidocarbonyl)phenyl, 5-amino-2-fluorophenyl, cyclopentylamidocarbonyl)phenyl, 3-amino-5-(Ncyclobutylamidocarbonyl)phenyl, 3-amino-5-(N-3-amino-5-hydroxymethylphenyl, 5-amino-3butyl) amidocarbonyl) phenyl, 3-amino-5-(N-

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diaminophenyl, 3-dimethylaminophenyl, 2-fluorophenyl, 3methoxyphenyl, 3-methoxyphenyl, 3-methoxyaminophenyl, 3carboxymethyl-5-hydroxyphenyl, 3-carboxymethylphenyl, 3methylphenyl, 5-amino-2-methylthiophenyl, 3-aminophenyl, 3-carboxyphenyl, 3-carboxy-5-aminophenyl, 3-carboxy-5fluorophenyl, 2,5-difluorophenyl, 2-hydroxyphenyl, 3methoxycarbonylphenyl, 3-amidinophenyl, 3-amino-2chlorophenyl, 2-chlorophenyl, 3-cyanophenyl, 3,5hydroxyphenyl, 3-carboxymethyl-5-aminophenyl, 3hydroxyphenyl, 3-methanesulfonylaminophenyl, 2methoxycarbonylphenyl, 2-methylaminophenyl, 3-

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methylaminophenyl, 2-methylphenyl, 3-methylphenyl, 4-

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methylphenyl, phenyl, 3-trifluoroacetamidophenyl, 3-trifluoromethylphenyl, 2-trifluoromethylphenyl, 5-amino-2-thienyl, 5-amino-3-thienyl, 3-bromo-2-thienyl, 3-pyridyl, 4-pyridyl, 2-thienyl, and 3-thienyl;

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Ris and Ris are independently selected from the group consisting of hydrido, amidino, amino, aminomethyl, methoxy, methylamino, hydroxy, hydroxymethyl, fluoro, chloro, and cyano;

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R¹⁷ and R¹⁸ are independently selected from the group consisting of hydrido, fluoro, chloro, hydroxy, hydroxymethyl, amino, carboxy, and cyano;

hydroxymethyl, amino, carboxy, and cyano; QP is C(NR25)NR32R24;

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 $R^{23},~R^{24},~and~R^{25}$ are independently hydrido or methyl; Q^{α} is CH_2 .

88. The compound of claim 87 or a pharmaceutically acceptable salt thereof, wherein;

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B is selected from the group consisting of hydrido, ethyl, 2-propenyl, 2-putyl, (R)-2-butyl, propyl, isopropyl, butyl, 2-butyl, (R)-2-butyl, tert-butyl, isobutyl, 1-pentyl, 3-pentyl, 2-methylbutyl, 2,2,2-trifluoroethyl, 6-amidocarbonylhexyl, 4-methyl-2-pentyl, 3-hydroxypropyl, 1-methoxy-2-propyl, 2-methyl-2-pentyl, 3-hydroxypropyl, 1-methyl-2-butyl, 2-dimethylaminopropyl, 2-cyanoethyl, 6-hydroxyhexyl, 2-hydroxyethyl, 2-amidinoethyl, 2-guanidinoethyl, 3-guanidinopropyl, 4-guanidinobutyl, 3-dimethylaminoethyl, 3-methylbutyl, 6-cyanohexyl, 2-methylbutyl, 3-aminopropyl, 2-hexyl, and 4-aminobutyl;

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A is selected from the group consisting of a bond, CH, CH,CH,CH and CH,CH;;

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hydroxy, amino, amidino, aminomethyl, cyano, methyl, trifluoromethyl, hydroxymethyl, and fluoro;

R' is selected from the group consisting of hydrido hydroxy, hydroxymethyl, amino, aminomethyl, cyano, methyl, trifluoromethyl, and fluoro;

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R² is selected from the group consisting of 3-amidocarbonyl-5-aminophenyl, 3-amino-5-(N-benzylamidocarbonyl)phenyl, 3-amino-5-(N-(2-chlorobenzyl)amidocarbonyl)phenyl, 3-amino-5-(N-(3-

fluorobenzyl) amidocarbonyl) phenyl, 3-amino-5-(N-(2-tifluoromethylbenzyl) amidocarbonyl) phenyl, 3-amino-5-(N-(1-phenylethyl) amidocarbonyl) phenyl, 3-amino-5-(N-(1-methyl-1-phenylethyl) amidocarbonyl) phenyl, 3-amino-5-(N-benzylamidosulfonyl) phenyl, 3-amino-5-(N-(2-tifluoryl)) phenyl, 3-amino-5-(N-(2-tifluoryl)) phenyl, 3-amino-5-(N-(2-tifluoryl)) phenyl, 3-amino-5-(N-(2-tifluoryl)) phenyl, 3-amino-5-(N-(2-tifluoryl)) phenyl, 3-amino-5-(N-(2-tifluoryl)) phenyl, 3-amino-5-(N-(3-tifluoryl)) phenyl, 3-amino-5-(N-(3-tifluoryl)) phenyl, 3-amino-5-(N-(3-tifluoryl)) phenyl)

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chlorobenzyl) amidosulfonyl)phenyl, 3-amino-5-(N-ethylamidocarbonyl)phenyl, 3-amino-5-(N-isopropylamidocarbonyl)phenyl, 3-amino-5-(N-propylamidocarbonyl)phenyl, 3-amino-5-(N-isobutylamidocarbonyl)phenyl, 3-amino-5-(N-isobutylamidocarbonyl)phenyl, 3-amino-5-(N-

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buty1) amidocarbony1) pheny1, 3-amino-5-(Ncyclobutylamidocarbony1) pheny1, 3-amino-5-(Ncyclopentylamidocarbony1) pheny1, 3-amino-5-(Ncyclohexylamidocarbony1) pheny1, 3-aminopheny1, 3-carboxy

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5-aminophenyl, 3-chlorophenyl, 3,5-diaminophenyl, 3-dimethylaminophenyl, 3-hydroxyphenyl, 3-methylaminophenyl, 2-methylaminophenyl, 3-methylaminophenyl, 2-methylaminophenyl, 3-methylaminophenyl, 3-acthylaminophenyl, 3-a

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methanesulfonylaminophenyl, 3-methylaminophenyl, 2methylphenyl, 3-methylphenyl, 3trifluoroacetamidophenyl, 3-bromo-2-thienyl, 2-thienyl,
and 3-thienyl;

y' is selected from the group consisting of 5-

amidinobenzyl, and 3-fluoro-4-amidinobenzyl. 89. The compound of Claim 82 wherein the compound

is selected from the group consisting of:

amidino-2-thienylmethyl, 4-amidinobenzyl, 2-fluoro-4-

or a pharmaceutically acceptable salt thereof, wherein; $R^2 \ is \ 3-aminophenyl, \ B \ is \ 2,2,2-trifluoroethyl, \ A \ is \ abond, \ Y^o \ is \ 4-amidinobenzyl, \ and \ R^1 \ is \ chloro;$

R² is 3-aminophenyl, B is (S)-2-butyl, A is a bond, Y° is 4-amidinobenzyl, and R² is chloro;

R' is 5-amino-2-fluorophenyl, B is isopropyl, A is a bond, Y° is 4-amidinobenzyl, and R' is chloro;
R' is 2-methyl-3-aminophenyl, B is isopropyl, A is a

bond, Y° is 4-amidinobenzyl, and R¹ is chloro;
R² is 3-aminophenyl, B is ethyl, A is a bond, Y° is

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4-amidinobenzyl, and R^1 is chloro; R^2 is 3-aminophenyl, B is ethyl, A is a bond, Y° is 4-amidino-2-fluorobenzyl, and R¹ is chloro;

 R^2 is 3-aminophenyl, B is 2-propenyl, A is a bond, Y° is 4-amidinobenzyl, and R^2 is chloro;

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R² is 3-aminophenyl, B is isopropyl, A is a bond, Y⁰

is 4-amidino-2-fluorobenzyl, and \mathbb{R}^1 is chloro; \mathbb{R}^2 is 3-aminophenyl, B is isopropyl, A is a bond, \mathbb{Y}^0

is 4-amidinobenzyl, and R^1 is chloro; $R^2 \text{ is 3-aminophenyl, B is 2-butyl, A is a bond, Y}^0 \text{ is 4-amidinobenzyl, and } R^1 \text{ is chloro};$

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 R^2 is 3-aminophenyl, B is (R)-2-butyl, A is a bond, $Y^{\rm o}$ is 4-amidinobenzyl, and $R^{\rm i}$ is chloro;

 $\rm R^2$ is 3-aminophenyl, B is 2-propynyl, A is a bond, Y° is 4-amidinobenzyl, and $\rm R^1$ is chloro;

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 R^2 is 3-aminophenyl, B is 3-pentyl, A is a bond, Y^{o} is 4-amidinobenzyl, and R^{i} is hydrido;

 $\rm R^2$ is 3-aminophenyl, B is hydrido, A is CH, Y° is 4-amidinobenzyl, and $\rm R^1$ is chloro,

 R^2 is 3-aminophenyl, B is ethyl, A is $CH_2,\ Y^0$ is 4-amidinobenzyl, and R^1 is chloro,

 R^2 is 3-aminophenyl, B is 2-methypropyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro;

 R^2 is 3-aminophenyl, B is 2-propyl, A is CH_1CH, Y^{α} is 4-amidinobenzyl, and R^1 is chloro;

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 R^2 is 3-aminophenyl, B is propyl, A is a bond, Υ^o is 4-amidino-2-fluorobenzyl, and R^1 is chloro,

 R^2 is 3-aminophenyl, B is 6-amidocarbonylhexyl, A is a bond, Υ^0 is 4-amidinobenzyl, and R^1 is chloro;

R² is 3-aminophenyl, B is text-butyl, A is a bond, Y^o is 4-amidinobenzyl, and R¹ is hydrido;

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 R^2 is 3-aminophenyl, B is tert-butyl, A is a bond, Y⁰ is 4-amidinobenzyl, and R¹ is chloro;

R' is 3-aminophenyl, B is 3-hydroxypropyl, A 18 a

bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro, R^2 is 3-aminophenyl, B is 2-methylpropyl, A is a

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bond, Y° is 4-amidino-2-fluorobenzyl, and R' is chloro; R' is 3-aminophenyl, B is butyl, A is a bond, Y° is 4-amidinobenzyl, and R' is chloro; R^2 is 3-aminophenyl, B is 1-methoxy-2-propyl, A is a bond, Y^o is 4-amidinobenzyl, and R^2 is chloro;

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 R^2 is 3-aminophenyl, B is 2-methoxyethyl, A is a bond, $Y^{\rm o}$ is 4-amidinobenzyl, and $R^{\rm i}$ is chloro;

 R^2 is 3-aminophenyl, B is 2-propyl, A is a bond, Y° is 5-amidino-2-thlenylmethyl, and R^2 is chloro;

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 R^2 is 5-amino-2-methylthiophenyl, B is 2-propyl, A is a bond, Y^o is 4-amidinobenzyl, and R^1 is chloro;

 R^2 is 3-amino-5-carboxyphenyl, B is isopropyl, A is a bond, Y° is 4-amidinobenzyl, and R^1 is chloro, R^2 is 3-amino-5-carbomethoxyphenyl, B is isopropyl, A

is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

 R^2 is 3-aminophenyl, B is isopropyl, A is a bond, $Y^{\rm o}$ is 4-amidinobenzyl, and \mathbb{R}^1 is bromo;

R² is 3-amino-5-carboxamidophenyl, B is isopropyl, A is a bond, Yo is 4-amidinobenzyl, and R1 is chloro;

methylamidocarbonyl)phenyl, B is isopropyl, A is a bond, Yo is 4-amidinobenzyl, and R1 is chloro; R2 is 3-amino-5-(N-benzyl-N-

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R² is 3-amino-5-(N-(1-

phenylethyl)amidocarbonyl)phenyl, B is isopropyl, A is a bond, Yo is 4-amidinobenzyl, and R1 is chloro;

R² is 3-amino-5-(N-(2-phenyl-2-

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propyl)amidocarbonyl)phenyl, B is isopropyl, A is a bond Y° is 4-amidinobenzyl, and R¹ is chloro;

R2 18 3-amino-5-(N-(2,4

dichlorobenzyl) amidocarbonyl) phenyl, B is isopropyl, A is a bond, Y° is 4-amidinobenzyl, and R1 is chloro; 15

is 3-amino-5-(N-(4-

bromobenzyl) amidocarbonyl) phenyl, B is isopropyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro;

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R² is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is isopropyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is

R2 is 3-amino-5-(N-(2-

chlorobenzyl) amidocarbonyl) phenyl, B is isopropyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

R2 is 3-amino-5-(N-(2-

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13 ۳, isopropyl, A is a bond, Y° is 4-amidinobenzyl, and trifluoromethylbenzyl)amidocarbonyl)phenyl, B is

R2 is 3-amino-5-(N-(3-

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B is isopropyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro; fluorobenzyl) amidocarbonyl) phenyl,

R2 is 3-amino-5-(N-(3-

isopropyl, A is a bond, Y^{o} is 4-amidinobenzyl, and R^{i} is trifluoromethylbenzyl)amidocarbonyl)phenyl, B is

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R2 is 3-amino-5-(N-isobutylamidocarbonyl) phenyl, B is isopropyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro;

R² is 3-amino-5-(N-cyclobutylamidocarbonyl)phenyl, B is isopropyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1

is chloro;

ø R² is 3-amino-5-(N-cyclopentylamidocarbonyl)phenyl, is isopropyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1

R² is 3-amino-5-(N-cycloheptylamidocarbonyl)phenyl, is chloro;

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is isopropyl, A is a bond, Y^{α} is 4-amidinobenzyl, and R^{1} is chloro;

R2 is 3-amino-5-(N-(2-

pyridylmethyl) amidocarbonyl) phenyl, B is isopropyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

R² is 3-amino-5-(N-(3-

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pyridylmethyl) amidocarbonyl) phenyl, B is isopropyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro;

R2 is 3-amino-5-(N-(2-(4-

methoxyphenyl)ethyl)amidocarbonyl)phenyl, B is isopropyl, A is a bond, Y^{o} is 4-amidinobenzyl, and R^{l} is chloro;

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phenylpropyl)amidocarbonyl)phenyl, B is isopropyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro; R2 is 3-amino-5-(N-(3-

R2 18 3-amino-5-(N-(2,2-

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diphenylethyl)amidocarbonyl)phenyl, B is isopropyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro;

R2 is 3-amino-5-(N-(2-

naphthylmethyl)amidocarbonyl)phenyl, B is isopropyl, A is R² is 3-amino-5-(N-(1,2,3,4-tetrahydronaphth-2a bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro,

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ylmethyl)amidocarbonyl)phenyl, B is isopropyl, A is

۶, R2 is 3-aminophenyl, B is 2-propyl, A is a bond, bond, Y° is 4-amidinobenzyl, and R^{1} is chloro;

 R^2 is 3-carboxyphenyl, B is 2-propyl, A is a bond, Y^0 is 4-amidino-3-fluorobenzyl, and R1 is hydrido; 33

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is 4-amidinobenzyl, and R1 is hydrido;

 R^2 is 3-aminophenyl, B is 2-propyl, A is a bond, Y° is 4-amidino-3-fluorobenzyl, and R1 is chloro; R² is 3,5-diaminophenyl, B is 2,2,2-trifluoroethyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

R² is 3,5-diaminophenyl, B is (S)-2-butyl, A is bond, Y° is 4-amidinobenzyl, and R¹ is chloro; R² is 3,5-diaminophenyl, B is isopropyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro; R' is 3,5-diaminophenyl, B is isopropyl, A is a bond, \mathbb{R}^2 is 3,5-diaminophenyl, B is ethyl, A is a bond, \mathbb{Y}^o Yo is 4-amidino-2-fluorobenzylbenzyl, and R1 is chloro; is 4-amidinobenzyl, and R1 is chloro;

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 R^2 is 3,5-diaminophenyl, B is ethyl, A is a bond, Y^o

4-amidino-2-fluorobenzyl, and R1 is chloro; 18

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trifluoroethyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 R² is 3-amino-5-carboxyphenyl, B is 2,2,2is chloro;

R² is 3-amino-5-carboxyphenyl, B is (S)-2-butyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

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R2 is 3-amino-5-carboxyphenyl, B is isopropyl, A is a bond, Y° is 4-amidino-2-fluorobenzylbenzyl, and R¹ is

R' is 3-amino-5-carboxyphenyl, B is ethyl, A is a bond, Yo is 4-amidinobenzyl, and R1 is chloro; chloro;

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bond, Y° is 4-amidino-2-fluorobenzyl, and R¹ is chloro; R' is 3-amino-5-carboxyphenyl, B is ethyl, A is a

2,2,2-trifluoroethyl, A is a bond, Y° is 4-amidinobenzyl, R2 is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is and R1 is chloro;

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(S)-2-butyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is R2 is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is

R² is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is isopropyl, A is a bond, Yo is 4-amidino-2-

fluorobenzylbenzyl, and R¹ is chloro,

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R² is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B 1s ethyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

ethyl, A is a bond, Y^0 is 4-amidino-2-fluorobenzyl, and R^1 R2 is 3-amino-5-(N-benzylamidocarbonyl)phenyl, is chloro;

R' is 3,5-diaminophenyl, B is isopropyl, A is a bond, Y° is 4-amidinobenzylbenzyl, and R¹ is hydrido.

The compound of claim 67 having the structure:

or a pharmaceutically acceptable salt thereof, wherein; M is N or N→O;

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carbons and a nitrogen adjacent to the carbon atom at the R13, a ring carbon or nitrogen adjacent to the R' position carbon at the point of attachment of B to A is optionally point of attachment are optionally substituted with R° or substituted with oxo provided that no more than one ring and two atoms from the point of attachment is optionally substituted with R10, a ring carbon or nitrogen adjacent substituted with R33, a ring carbon other than the ring heterocyclyl, wherein each ring carbon is optionally carbon is substituted by oxo at the same time, ring to the R13 position and two atoms from the point of B is a C3-C7 cycloalkyl or a C4-C6 saturated

atoms from the point of attachment and adjacent to the R^{12} attachment and adjacent to the \mathbb{R}^{10} position is optionally substituted with R11, a ring carbon or nitrogen three attachment is optionally substituted with R12, a ring carbon or nitrogen three atoms from the point of

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position is optionally substituted with R33, and a ring attachment and adjacent to the R11 and R13 positions is carbon or nitrogen four atoms from the point of optionally substituted with R34;

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R, R11, and R13 are independently selected from the group consisting of hydrido, hydroxy, amino, amidino, guanidino, alkylamino, alkylthio, alkylsulfonamido, alkylsulfinyl, alkylsulfonyl, amidosulfonyl, alkyl, alkoxy, halo, haloalkyl, haloalkoxy, hydroxyalkyl, hydroxyhaloalkyl, carboxy, carboxamido, and cyano; R10 and R12 are independently selected from the group amidino, guanidino, alkyl, aryl, aralkyl, cycloalkyl, alkylamino, arylamino, aralkylamino, heteroarylamino, cycloalkylalkyl, heteroaryl, heterocyclyl, alkoxy, cycloalkoxy, cycloalkylalkoxy, aralkoxy, aryloxy, consisting of hydrido, acetamido, haloacetamido, heterocyclylalkoxy, hydroxy, amino, alkoxyamino, heteroaryloxy, heteroaralkoxy,heterocyclyloxy, heteroaralkylamino, heterocyclylamino,

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heterocyclylalkylamino, alkylsulfonamido, amidosulfonyl, carboxyalkyl, carboxamido, halo, haloalkyl, and cyano; sycloalkylsulfonyl, heteroarylsulfonyl, hydroxyalkyl, hydroxyhaloalkyl, aminoalkyl, carboalkoxy, carboxy, arylsulfinyl, aralkylsulfinyl, cycloalkylsulfinyl, heteroarylsulfinyl, aryløulfonyl, aralkylsulfonyl,

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R14 is selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkoxy, nydroxyalkyl, hydroxyhaloalkyl, carboalkoxy, carboxy, hydroxy, amino, alkoxyamino, alkylamino, alkylthio, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy, carboxamido, and cyano;

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R13 is selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkoxy, nydroxyalkyl, hydroxyhaloalkyl, carboalkoxy, carboxy, hydroxy, amino, alkoxyamino, alkylamino, alkylthio, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy,

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carboxamido, cyano, and Qb;

A is a bond or (CH(Ris)) $_{pa}$ - (W7) $_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W' is (R')NC(0) or N(R'); R' is selected from the group consisting of hydrido, hydroxy and alkyl;

R15 is selected from the group consisting of hydrido, halo, alkyl, and haloalkyl;

Ja is N or C-Xº;

Jb is N or C-R1;

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R¹ and X° are independently selected from the group consisting of hydrido, hydroxy, hydroxyamino, amidino, amino, cyano, hydroxyalkyl, alkoxy, alkyl, alkylamino, aminoalkyl, alkylthio, alkoxyamino, haloalkyl,

haloalkoxy, and halo;

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R2 18 Z0-0;

Z° is selected from the group consisting of a bond, selected from the group consisting of 0, S, and N(R*1); CH_2 , CH_2CH_2 , $W^0-\left(CH\left(R^{42}\right)\right)_p$ wherein p is 0 or 1 and W^0 is

R' and R' are independently hydrido or alkyl;

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optionally substituted by R', the other carbon adjacent to substituted by R12, and any carbon adjacent to both R10 and from the carbon at the point of attachment is optionally substituted by R10, a carbon adjacent to R13 and two atoms from the carbon at the point of attachment is optionally Q is phenyl or a heteroaryl of 5 or 6 ring members, substituted by R13, a carbon adjacent to R9 and two atoms wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to 2° is the carbon at the point of attachment is optionally R12 is optionally substituted by R11;

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Y° is phenyl or a heteroaryl of 5 or 6 ring members, substituted by Q°, a carbon two or three atoms from the wherein one carbon of said phenyl or said heteroaryl is point of attachment of Q' to said phenyl or said

heteroaryl is substituted by $Q^{\mathtt{b}}$, a carbon adjacent to the

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point of attachment of Q" is optionally substituted by R¹⁷, is optionally substituted by R¹⁸, a carbon adjacent to Q^b another carbon adjacent to the point of attachment of Q* is optionally substituted by Rig, and another carbon adjacent to Q^b is optionally substituted by R¹⁹;

 R^{17} and R^{18} are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano;

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R16 and R19 are selected from the group consisting of:

alkylthio, alkyleulfinyl, alkyleulfonyl, alkanoyl, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, (i) hydrido, amidino, guanidino, carboxy, hydroxyalkyl, aminoalkyl, and cyano; and

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 \mathbb{Q}^{\flat} is selected from the group consisting of $NR^{20}R^{21}$, (ii) NR20R21 or and C(NR25)NR21R24, with the proviso that R16, R19, and QD are not simultaneously hydrido;

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- with the further proviso that no more than one of \mathbb{R}^{13} and hydrido, and C(NR28)NR21R24, with the proviso that no more than one of R20 and R21 is hydroxy at the same time and R24 is hydroxy at the same time;
- from the group consisting of hydrido, alkyl, and hydroxy; R20, R21, R21, R24, and R25 are independently selected O' is selected from the group consisting of a bond, CH, and CH, CH,.

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91. The compound of claim 90 or a pharmaceutically acceptable salt thereof, wherein;

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M is N or N→O;

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azetidin-2-yl, azetidin-3-yl, thiaetan-3-yl, cyclopentyl, cyclohexyl, norbornyl, 7-oxabicyclo[2.2.1]heptan-2-yl, cyclopropyl, cyclobutyl, oxetan-3-yl, azetidin-1-yl, B is selected from the group consisting of

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bicyclo[3.1.0]hexan-6-yl, cycloheptyl, 2-morpholinyl, 3-

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pyrrolidinyl, 2-dioxanyl, 4H-2-pyranyl, 4H-3-pyranyl, 4Hmorpholinyl, 4-morpholinyl, 1-piperazinyl, 2-piperazinyl, 4-pyranyl, 4H-pyran-4-one-2-yl, 4H-pyran-4-one-3-yl, 2piperidinyl, 1-pyrrolidinyl, 2-pyrrolidinyl, 3-1-piperidinyl, 2-piperidinyl, 3-piperidinyl, 4tetrahydropyranyl, 2-tetrahydrothienyl, and 3tetrahydropyranyl, 3-tetrahydropyranyl, 4tetrahydrofuranyl, 3-tetrahydrofuranyl, 2-

substituted with R33, ring carbons and a nitrogen adjacent tetrahydrothienyl, wherein each ring carbon is optionally nitrogen adjacent to the R' position and two atoms from the point of attachment is optionally substituted with position and two atoms from the point of attachment is optionally substituted with R9 or R13, a ring carbon or R^{10} , and a ring carbon or nitrogen adjacent to the R^{13} to the carbon atom at the point of attachment are optionally substituted with R12;

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group consisting of hydrido, amidino, guanidino, carboxy, isopropoxy, propoxy, hydroxy, amino, N-methylamino, N,Nisopropylthio, trifluoromethyl, pentafluoroethyl, 2,2,2-R', R'1, and R'3 are independently selected from the hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 2,2,2chloro, bromo, methanesulfonamido, amidosulfonyl, Ntrifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, methylamidocarbonyl, N,N-dimethylamidocarbonyl, and dimethylamino, N-ethylamino, methylthio, ethylthio, methyl, ethyl, propyl, isopropyl, methoxy, ethoxy, methylamidosulfonyl, N,N-dimethylamidosulfonyl, trifluoroethyl, 2,2,3,3,3-pentafluoropropyl, trifluoro-1-hydroxyethyl, amidocarbonyl, N-

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carboxymethyl, methyl, ethyl, propyl, isopropyl, methoxy, R^{10} and R^{12} are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, ethoxy, isopropoxy, propoxy, hydroxy, amino,

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phenylethyl)amidocarbonyl, N-benzylamidosulfonyl, N-(2-N.N-dimethylamidosulfonyl, hydroxymethyl, 1-hydroxyethyl, methanesulfonamido, amidosulfonyl, N-methylamidosulfonyl benzylamidocarbonyl, N-(2-chlorobenzyl)amidocarbonyl, Nsyclobutylamidocarbonyl, N-cyclopentylamidocarbonyl, Nbenzyloxy, 4-bromo-3-fluorophenoxy, 3-bromobenzyloxy, 4· aminoethyl, N-methylamino, dimethylamino, N-ethylamino, crifluoromethycyclohexylmethoxy, cyclopentoxy, benzyl, cyclohexylamidocarbonyl, fluoro, chloro, bromo, cyano, chlorobenzyl)amidosulfonyl, N-ethylamidocarbonyl, N-/lmethylamino, 4-butoxyphenamino, 3-chlorobenzyl, 4bromobenzyloxy, 4-bromobenzylamino, 5-bromopyrid-2-.sobutylamidocarbonyl, N-(2-butyl)amidocarbonyl, Nchlorophenoxy, 4-chloro-3-ethylphenoxy, 4-chloro-3methoxycarbonyl, ethoxycarbonyl, amidocarbonyl, Nmethylamidocarbonyl, N,N-dimethylamidocarbonyl, Nsopropylamidocarbonyl, N-propylamidocarbonyl, Nethylbenzylamino, 4-chloro-3-ethylphenylamino, 3trifluoroacetamido, aminomethyl, 1-aminoethyl, 2cyclobutoxy, cyclohexoxy, cyclohexylmethoxy, 4chlorophenylsulfonyl, 5-chloropyrid-3-yloxy, 2cyanopyrid-3-yloxy, 2,3-difluorobenzyloxy, 2,4-2-hydroxyethyl, 2,2,2-trifluoro-1-hydroxyethyl, chlorobenzylsulfonyl, 4-chlorophenylamino, 4-:rifluoromethylbenzyl) amidocarbonyl, N-(1phenylethyl)amidocarbonyl, N-(1-methyl-1chlorobenzyloxy, 4-chlorobenzyloxy, 4ethoxyamino, acetamido, (3-fluorobenzyl)amidocarbonyl, N-(2methoxyamino, ഗ 10 15 20 25

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 R^{33} is selected from the group consisting of hydrido, chloro, bromo, amidosulfonyl, N-methylamidosulfonyl, N,Namidino, guanidino, carboxy, methoxy, ethoxy, isopropoxy, dimethylamidosulfonyl, hydroxymethyl, 1-hydroxyethyl, 2isopropylthio, trifluoromethyl, pentafluoroethyl, 2,2,2methylphenoxy, 4-isopropylbenzyloxy, 3-isopropylphenoxy, 3-trifluoromethoxyphenoxy, 4-trifluoromethoxyphenoxy, 3trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-2,3,5-trifluorophenoxy, 3-pentafluoroethylphenoxy, 3trifluoromethylbenzyloxy, 4-trifluoromethylbenzyloxy, trifluoromethylthiobenzyloxy, 2,3,4-trifluorophenoxy, isopropylphenoxy, 4-isopropylphenoxy, 4-isopropyl-3propoxy, hydroxy, amino, methoxyamino, ethoxyamino, fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2trifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, phenylethyl, 2-phenylethylamino, phenylsulfonyl, 3dimethylamino, N-ethylamino, methylthio, ethylthio, fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4trifluoromethylphenoxy, 4-isopropylbenzyloxy, 3-4-isopropylphenoxy, 4-isopropyl-3-methylphenoxy, phenylamino, 1-phenylethoxy, 2-phenylethoxy, 2methylphenoxy, 4-fluorobenzyloxy, 2-fluoro-3trifluoromethylbenzyloxy, 2-fluorophenoxy, 4ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5acetamido, trifluoroacetamido, N-methylamino, trifluoroethyl, 2,2,3,3,3-pentafluoropropyl, (1,1,2,2-tetrafluoroethoxy) phenoxy, and 3trifluoromethylbenzyloxy, 4-fluoro-3trifluoromethylbenzyloxy, 3-fluoro-5trifluoromethylbenzyloxy, 4-fluoro-2-2,4-bis-trifluoromethylbenzyloxy, 3trifluoromethylthiobenzyloxy, 4trifluoromethylthiophenoxy; 10 15 20 30 35 25

hydroxyethyl, 2,2,2-trifluoro-1-hydroxyethyl,

iimethylbenzyloxy, 4-ethoxyphenoxy, 4-ethylbenzyloxy, 3-

dimethylphenoxy, 3,4-dimethylbenzyloxy, 3,5-

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difluorobenzyloxy, 4-difluoromethoxybenzyloxy, 2,3-

difluorophenoxy, 2,4-difluorophenoxy, 2,5difluorophenoxy, 3,5-dimethylphenoxy, 3,4-

difluorobenzyloxy, 3,4-difluorobenzyloxy, 2,5-

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difluorobenzyloxy, 3,5-difluorophenoxy, 3,5-

methoxycarbonyl, ethoxycarbonyl, amidocarbonyl, N-methylamidocarbonyl, N.N-dimethylamidocarbonyl, cyano, and $Q^{\flat}\,;$

Ja is Nor C-X°;

Jb is N or C-R1;

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R¹ and X° are independently selected from the group consisting of hydrido, hydroxy, amino, amidino, hydroxyamino, aminomethyl, 1-aminoethyl, methylamino, dimethylamino, cyano, methyl, ethyl, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, methoxy, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, methoxyamino, methylthio, ethylthio, trifluoromethoxy, 1,1,2,2-tetrafluoroethoxy, fluoro, chloro, and bromo;

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R2 18 Z0-Q;

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Z° is selected from the group consisting of a bond, CH₂, CH₂CH₂, O, S, NH, N(CH₃), OCH₂, SCH₂, N(H)CH₂, and N(CH₃)CH₂;

Q is selected from the group consisting of phenyl, 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3-pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-pyrazolyl, 4-pyrazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 4-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-pyrazinyl, 2-pyridyl, 2-pyrimidinyl, 2-pyrimidinyl, 2-pyrimidinyl, 3-pyridazinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, 6-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, 5-pyrimidinyl, 3-pyridazinyl, 6-pyridazinyl, 5-pyrimidinyl, 3-pyridazinyl, 6-pyridazinyl, 5-pyrimidinyl, 3-pyridazinyl, 6-pyridazinyl, 6-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, 6-pyridazinyl, 6-pyrimidinyl, 9-pyrimidinyl, 9-pyrimidinyl, 9-pyridazinyl, 6-pyridazinyl, 6-pyridazinyl, 6-pyridazinyl, 6-pyridazinyl, 6-pyridazinyl, 6-pyridazinyl, 8-pyridazinyl, 8-pyrid

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point of attachment is optionally substituted by R^{12} , and any carbon adjacent to both R^{10} and R^{12} is optionally substituted by R^{11} ;

Yo is selected from the group consisting of:

1-Q^b-4-Q^a-2-R¹⁴-3-R¹⁷-5-R¹⁸-6-R¹⁹benzene, 2-Q^b-5-Q^a-6-R¹⁷-4-R¹⁸-3-R¹⁸pyridine, 3-Q^b-6-Q^a-2-R¹⁸-5-R¹⁸-4-R¹⁸pyridine, 2-Q^b-5-Q^a-3-R¹⁸-5-R¹⁸-4-R¹⁸pyridazine, 2-Q^b-6-Q^a-2-R¹⁸pyrimidine, 5-Q^b-2-Q^a-4-R¹⁷-6-R¹⁸pyrimidine, 5-Q^b-2-Q^a-4-R¹⁸-6-R¹⁸pyrimidine, 3-Q^b-5-Q^a-4-R¹⁸-2-R¹⁸pyrimidine, 2-Q^b-5-Q^a-3-R¹⁸-4-R¹⁷thiophene, 3-Q^b-5-Q^a-4-R¹⁸-2-R¹⁸pyrrole, 2-Q^b-5-Q^a-3-R¹⁸-4-R¹⁹pyrrole, 4-Q^b-5-Q^a-3-R¹⁸-4-R¹⁹pyrrole, 2-Q^b-6-R¹⁸-1-R

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 R^{19} thiazole, and 2- Q^{b} -5- Q^{a} -4- R^{17} thiazole;

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R¹⁷ and R¹⁹ are independently selected from the group consisting of hydrido, methyl, ethyl, isopropyl, propyl, carboxy, amidino, guanidino, methoxy, ethoxy, isopropoxy, propoxy, hydroxy, amino, aminomethyl, 1-aminoethyl, 2-aminoethyl, N-methylamino, dimethylamino, N-ethylamino, methylthio, ethylthio, isopropylthio,

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methyltnio, ethyltnio, isopropromio,
trifluoromethylthio, methylsulfinyl, ethylsulfinyl,
methylsulfonyl, ethylsulfonyl, trifluoromethyl,
pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3-

pentafluoropropyl, trifluoromethoxy, 1,1,2,2tetrafluoroethoxy, fluoro, chloro, bromo, hydroxymethyl,
1-hydroxyethyl, 2-hydroxyethyl, and cyano;

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R¹⁶ and R¹⁹ are selected from the group consisting of:
(1) hydrido, methyl, ethyl, isopropyl, propyl,
carboxy, amidino, guanidino, methoxy, ethoxy, isopropoxy,
propoxy, hydroxy, amino, aminomethyl, 1-aminoethyl, 2aminoethyl, N-methylamino, dimethylamino, N-ethylamino,
methylthio, ethylthio, isopropylthio,

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trifluoromethylthio, methylsulfinyl, ethylsulfinyl,
methylsulfonyl, ethylsulfonyl, trifluoromethyl,
pentafluoroethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3-

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tetrafluoroethoxy, fluoro, chloro, bromo, hydroxymethyl 1-hydroxyethyl, 2-hydroxyethyl, and cyano; and pentafluoropropyl, trifluoromethoxy, 1,1,2,2-

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(ii) C(NR25)NR21R24 with the proviso that R16, R19, and Qb are not simultaneously hydrido;

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Qb is C(NR25)NR23R24 or hydrido, with the proviso that no more than one of \mathbb{R}^{23} and \mathbb{R}^{24} is hydroxy at the same

group consisting of hydrido, methyl, ethyl, and hydroxy; R^{23} , R^{24} , and R^{25} are independently selected from the Q° is selected from the group consisting of a bond, CH, and CH,CH,.

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92. The compound of claim 91 or a pharmaceutically acceptable salt thereof, wherein;

M is N→O;

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cycloheptyl, oxalan-2-yl, 2-(2R)-bicyclo[2.2.1]-heptyl, 1-pyrrolidinyl, 1-piperidinyl, oxetan-3-yl, azetidin-1cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, B is selected from the group consisting of

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piperazinyl, 2-piperazinyl, 1-piperidinyl, 2-piperidinyl, pyrrolidinyl, 3-pyrrolidinyl, 2-dioxanyl, 4H-2-pyranyl, oxabicyclo[2.2.1]heptan-2-yl, bicyclo[3.1.0]hexan-6-yl, 4H-3-pyranyl, 4H-4-pyranyl, 4H-pyran-4-one-2-yl, 4H-3-piperidinyl, 4-piperidinyl, 1-pyrrolidinyl, 2-2-morpholinyl, 3-morpholinyl, 4-morpholinyl, 1pyran-4-one-3-yl, 2-tetrahydrofuranyl, 3yl, azetidin-2-yl, azetidin-3-yl, 7-

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A is selected from the group consisting of a bond, tetrahydrothienyl, and 3-tetrahydrothienyl; tetrahydrofuranyl, 2-tetrahydropyranyl, 3tetrahydropyranyl, 4-tetrahydropyranyl, 2-

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Ja is N or C-Xº;

NHC(0), CH2CH2, and CH2CH2H

Jb is N or C-R1;

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R' and X° are independently selected from the group

hydroxyamino, aminomethyl, methylamino, cyano, methyl, trifluoromethyl, methoxy, hydroxymethyl, methoxyamino, methylthio, trifluoromethoxy, fluoro, and chloro; consisting of hydrido, hydroxy, amino, amidino,

R2 18 Z0-Q;

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Z° is selected from the group consisting of a bond, O, S, NH, N(CH₃), OCH₂, and SCH₂;

benzylaminophenyl, 3-amino-5-(2-phenylethylamino)phenyl benzylamidocarbonyl)phenyl, 3-amino-5-benzylphenyl, 3-Q is selected from the group consisting of 3amidocarbonyl-5-aminophenyl, 3-amino-5-(Namino-5-(2-phenylethyl)phenyl, 3-amino-5-3-amino-5-benzyloxyphenyl, 3-amino-5-(2phenylethoxy) phenyl, 3-amino-5-(N-(2-

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chlorobenzyl) amidocarbonyl) phenyl, 3-amino-5-(N-(3fluorobenzyl)amidocarbonyl)phenyl, 3-amino-5-(N-(2-

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trifluoromethylbenzyl)amidocarbonyl)phenyl, 3-amino-5-(Nmethyl-1-phenylethyl) amidocarbonyl) phenyl, 3-amino-5-(N-(1-phenylethyl)amidocarbonyl)phenyl, 3-amino-5-(N-(1benzylamidosulfonyl)phenyl, 3-amino-5-(N-(2-

chlorobenzyl) amidosulfonyl) phenyl, 3-amino-5-(Nisopropylamidocarbonyl)phenyl, 3-amino-5-(Nethylamidocarbonyl)phenyl, 3-amino-5-(N-

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isobutylamidocarbonyl)phenyl, 3-amino-5-(N-(2cyclobutylamidocarbonyl)phenyl, 3-amino-5-(Noutyl)amidocarbonyl)phenyl, 3-amino-5-(N-

propylamidocarbonyl)phenyl, 3-amino-5-(N-

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cyclohexylamidocarbonyl)phenyl, 5-amino-2-fluorophenyl, cyclopentylamidocarbonyl)phenyl, 3-amino-5-(N-3-amino-5-hydroxymethylphenyl, 5-amino-3-

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5-(4-trifluoromethylbenzyloxy)phenyl, 3-carboxyphenyl, 3-3-amino-5-(4-trifluoromethylbenzylamino)phenyl, 3-aminomethylphenyl, 5-amino-2-methylthiophenyl, 3-aminophenyl, carboxy-5-hydroxyphenyl, 3-amino-5-carboxyphenyl, 3methoxycarbonylphenyl, 3-amidinophenyl, 3-amino-2chlorophenyl, 2-chlorophenyl, 3-cyanophenyl, 3,5-35

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diaminophenyl, 3-dimethylaminophenyl, 2-fluorophenyl, 3-fluorophenyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 3-methanesulfonylaminophenyl, 2-methoxyphenyl, 3-methoxyphenyl, 3-methoxyphenyl, 3-methoxycarbonylphenyl, 2-methylaminophenyl, 3-methylaminophenyl, 3-methylphenyl, 3-methylphenyl, 3-trifluoroacetamidophenyl, 3-trifluoromethylphenyl, 3-trifluoromethylphenyl, 5-amino-2-thienyl, 5-amino-2-thienyl, 3-pyridyl, 4-pyridyl, 2-thienyl, and 3-thienyl, 3-pyridyl, 2-thienyl, and 3-thienyl;

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 Y^o is selected from the group consisting of: $1-Q^b-4-Q^a-2-R^{16}-3-R^{17}-5-R^{18}-6-R^{19} benzene, \ 2-Q^b-5-Q^a-6-R^{17}-4-R^{18}-3-R^{19}pyridine, \ 3-Q^b-6-Q^a-2-R^{16}-5-R^{18}-4-R^{19}pyridine, \ 3-Q^b-6-Q^a-3-R^{16}-5-R^{16}-3-R^{16}-3-R^{16}-1-R^{19}pyridine, \ 3-Q^a-4-R^{16}-3-R^{16}-1-R^{19}$

Ris and Ris are selected from the group consisting of:

(i) hydrido, amidino, aminomethyl, methoxy,
methylamino, hydroxy, hydroxymethyl, fluoro, chloro, and
cyano,

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Cyano,

(ii) C(NR²⁵)NR²¹R²⁴ with the proviso that R¹⁶, R¹⁹, and

Q^b are not simultaneously hydrido;

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R¹⁷ and R¹⁸ are independently selected from the group consisting of hydrido, fluoro, chloro, hydroxy, hydroxymethyl, amino, carboxy, and cyano;

 \mathbb{Q}^b is C(NR²³)NR²³R²⁴ or hydrido; · R²³, R²⁴, and R²⁵ are independently hydrido or methyl; \mathbb{Q}^e is CH.

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93. The compound of claim 90 having the structure:

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or a pharmaceutically acceptable salt thereof, wherein;

B is a C3-C7 cycloalkyl or a C4-C6 saturated heterocyclyl, wherein each ring carbon is optionally substituted with R³, a ring carbon other than the ring carbon at the point of attachment of B to A is optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbons and a nitrogen adjacent to the carbon atom at the point of attachment are optionally substituted with R³ or R³, a ring carbon or nitrogen adjacent to the R³ position and two atoms from the point of attachment is optionally substituted with R³, a ring carbon or nitrogen adjacent to the R³ position and two atoms from the point of attachment is optionally substituted with R³, a ring carbon or nitrogen three atoms from the point of attachment and adjacent to the R³ position is optionally

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substituted with R¹¹, a ring carbon or nitrogen three atoms from the point of attachment and adjacent to the R¹² position is optionally substituted with R¹³, and a ring carbon or nitrogen four atoms from the point of attachment and adjacent to the R¹¹ and R¹³ positions is optionally substituted with R¹⁴,

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 $R^9,\ R^{11},$ and R^{13} are independently selected from the group consisting of hydrido, hydroxy, amino, amidino, guanidino, alkylamino, alkylthio, alkylsulfinyl,

alkylsulfonyl, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, carboxy, carboxamido, and cyano; R¹⁰ and R¹² are independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkyl, alkoxy, alkoxyamino, hydroxy, amino, alkylsulfonamido, amidosulfonyl, hydroxyalkyl, aminoalkyl, halo, haloalkyl, carboalkoxy, carboxamido, carboxyalkyl, and cyano;

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R³⁴ is independently selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkoxy, hydroxy, amino, alkoxyamino, alkylthio, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, carboalkoxy, carboxamido, and cyano;

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R³³ is selected from the group consisting of hydrido, acetamido, haloacetamido, amidino, guanidino, alkoxy, hydroxy, amino, alkoxyamino, alkylamino, alkylthio, amidosulfonyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, carboalkoxy, carboxamido, cyano and Q^b;

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A is a bond or $(CH(R^{15}))_{pa}-(W^7)_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W is $N(R^7)$;

R' is hydrido or alkyl;

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 R^{15} is selected from the group consisting of hydrido, halo, alkyl, and haloalkyl;

R₁ and X° are independently selected from the group consisting of hydrido, hydroxy, hydroxyamino, amidino, amino, cyano, hydroxyalkyl, alkoxy, alkyl, alkylamino, aminoalkyl, alkylthio, alkoxyamino, haloalkyl, and halo,

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R2 18 Z0-Q;

Z° is a bond;

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Q is phenyl or a heteroaryl of 5 or 6 ring members, wherein a carbon adjacent to the carbon at the point of

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attachment of said phenyl or heteroaryl ring to Z^0 is optionally substituted by R^2 , the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R^{13} , a carbon adjacent to R^2 and two atoms from the carbon at the point of attachment is optionally substituted by R^{19} , a carbon adjacent to R^{13} and two atoms from the carbon at the point of attachment is optionally substituted by R^{12} , and any carbon adjacent to both R^{10} and R^{12} is optionally substituted by R^{11} ;

 Y^o is phenyl or a heteroaryl of 5 or 6 ring members, wherein one carbon of said phenyl or said heteroaryl is substituted by Q^a , a carbon two or three atoms from the point of attachment of Q^a to said phenyl or said heteroaryl is substituted by Q^b , a carbon adjacent to the point of attachment of Q^a is optionally substituted by R^{19} , another carbon adjacent to the point of attachment of Q^a is optionally substituted by R^{19} , a carbon adjacent to Q^b is optionally substituted by R^{19} , and another carbon adjacent to Q^b is optionally substituted by R^{19} ;

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R¹⁷ and R¹⁸ are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, alkylthio, alkylsulfinyl, alkylsulfinyl, alkylsulfinyl, haloalkyl, haloalkoxy, hydroxy, aminoalkyl, and ovano.

hydroxyalkyl, aminoalkyl, and cyano; Ri* and Ri* are selected from the group consisting of:

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(i) hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, haloalkyl, haloalkoxy,

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hydroxyalkyl, aminoalkyl, and cyano; and (11) NR²⁰R²¹ or C(NR²⁵)NR²³R²⁴, with the proviso that R¹⁶, R¹⁵, and Q² are not simultaneously hydrido;

 \mathbb{Q}^b is selected from the group consisting of $NR^{10}R^{21}$, hydrido, and $C(NR^{25})\,NR^{23}R^{24}$;

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R20, R21, R21, R24, and R25 are independently hydrido or

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Q" is CH2. alkyl;

The compound of claim 93 or a pharmaceutically acceptable salt thereof, wherein;

 \mathfrak{L}^{10} , and a ring carbon or nitrogen atom adjacent to the \mathbb{R}^{13} tetrahydrothienyl, wherein each ring carbon is optionally substituted with R¹³, ring carbons and a nitrogen adjacent oxetan-3-yl, azetidin-1-yl, azetidin-2-yl, azetidin-3-yl, otperidinyl, 2-piperidinyl, 3-piperidinyl, 4-piperidinyl, nydrido, methyl, ethyl, methoxy, ethoxy, hydroxy, amino, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, the point of attachment are optionally substituted with nitrogen adjacent to the R' position and two atoms from cycloheptyl, oxalan-2-yl, 2-(2R)-bicyclo[2.2.1]-heptyl, bicyclo[3.1.0]hexan-6-yl, 2-morpholinyl, 3-morpholinyl, position and two atoms from the point of attachment is optionally substituted with R^9 or R^{13} , a ring carbon or dioxanyl, 2-tetrahydrofuranyl, 3-tetrahydrofuranyl, 2ndependently selected from the group consisting of optionally substituted with R¹²; R³; R¹¹, and R¹³ are to the carbon atom at the point of attachment are cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, lydroxymethyl, 1-hydroxyethyl, amidocarbonyl, N--morpholinyl, 1-piperazinyl, 2-piperazinyl, 1-B is selected from the group consisting of -pyrrolidinyl, 2-pyrrolidinyl, 3-pyrrolidinyl, methylamidosulfonyl, N,N-dimethylamidosulfonyl, tetrahydropyranyl, 2-tetrahydrothienyl, and 3-N-methylamino, N,N-dimethylamino, methylthio, tetrahydropyranyl, 3-tetrahydropyranyl, 4methylamidocarbonyl, carboxy, and cyano; fluoro, chloro, bromo, amidosulfonyl, N-

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R10 and R12 are independently selected from the group consisting of hydrido, amidino, amidocarbonyl, Nmethylamidocarbonyl, N-benzylamidocarbonyl, N-(2-

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N- (2-2-hydroxyethyl, carboxy, carboxymethyl, amino, acetamido, cyclobutylamidocarbonyl, N-cyclopentylamidocarbonyl, Nmethoxy, ethoxy, hydroxy, hydroxymethyl, 1-hydroxyethyl, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, chlorobenzyl)amidosulfonyl, N-ethylamidocarbonyl, Nmethanesulfonamido, methoxycarbonyl, fluoro, chloro, 1sobutylamidocarbonyl, N-(2-butyl)amidocarbonyl, Nphenylethyl)amidocarbonyl, N-benzylamidosulfonyl, cyclohexylamidocarbonyl, guanidino, methyl, ethyl, isopropylamidocarbonyl, N-propylamidocarbonyl, Nmethylamidosulfonyl, N,N-dimethylamidosulfonyl, trifluoroacetamido, aminomethyl, N-methylamino, dimethylamino, methoxyamino, amidosulfonyl, Ntrifluoromethylbenzyl)amidocarbonyl, N-(1phenylethyl) amidocarbonyl, N-(1-methyl-1chlorobenzyl) amidocarbonyl, N-(3fluorobenzyl) amidocarbonyl, N-(2-15 10

bromo, and cyano;

R¹¹ is selected from the group consisting of hydrido, pentafluoroethyl, 2,2,2-trifluoroethyl, fluoro, chloro, nydroxy, carboxy, amino, N-methylamino, dimethylamino, methoxyamino, methylthio, ethylthio, trifluoromethyl, amidino, guanidino, methyl, ethyl, methoxy, ethoxy, bromo, amidosulfonyl, N-methylamidosulfonyl, hydroxymethyl, amidocarbonyl, cyano, and $Q^b;$

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X° is selected from the group consisting of hydrido, A is selected from the group consisting of a bond, hydroxy, amino, amidino, aminomethyl, cyano, methyl, NH, N(CH₃), CH₂, CH₃CH, CH₂CH₂, and CH₂CH₂CH₃;

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R' is selected from the group consisting of hydrido, hydroxy, hydroxymethyl, amino, aminomethyl, methylamino, cyano, methyl, trifluoromethyl, methoxy, methylthio, trifluoromethyl, hydroxymethyl, chloro, and fluoro; trifluoromethoxy, fluoro, and chloro;

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R' is selected from the group consisting of phenyl, 2-thienyl, 2-furyĺ, 2-pyrrolyl, 2-imidazolyl, 2-

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is optionally substituted by R^{10} , a carbon adjacent to R^{13} and two atoms from the carbon at the point of attachment is optionally substituted by R¹², and any carbon adjacent is optionally substituted by R^{13} , a carbon adjacent to R^9 and two atoms from the carbon at the point of attachment pyridine ring is optionally substituted by R3, the other carbon adjacent to the carbon at the point of attachment wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to the to both R^{10} and R^{12} is optionally substituted by R^{11} ; thiazolyl, 3-isoxazolyl, 2-pyridyl, and 3-pyridyl,

3-Qb-5-Q°-4-R16-2-R19furan, 2-Qb-5-Q8-3-R16-4-R17furan, 3-Qb-5-Q*-4-R16-2-R19pyrrole, 2-Q^b-5-Q"-3-R16-4-R1pyrrole, 4-Q^b-2-Q"-1-Qb-4-Qe-2-R16-3-R17-5-R18-6-R19benzene, 2-Qb-5-Q-6-R17-4-R16-3-R19pyridine, 2-Qb-5-Q6-3-R16-4-R17thiophene, 3-Qb-6-Q*-2-R15-5-R18-4-R19pyridine, 3-Qb-5-Q*-4-R18-2-R19thiophene, Yo is selected from the group consisting of: 5-R19thiazole, and 2-Q5-5-Q-4-R17thiazole;

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 R^{16} , R^{17} , R^{19} , and R^{19} are independently selected from pentafluoroethyl, 2,2,2-trifluoroethyl, trifluoromethoxy, the group consisting of hydrido, methyl, ethyl, amidino, aminoethyl, 2-aminoethyl, N-methylamino, dimethylamino, guanidino, methoxy, hydroxy, amino, aminomethyl, 1methylsulfinyl, methylsulfonyl, trifluoromethyl, methylthio, ethylthio, trifluoromethylthio,

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from the group consisting of hydrido, methyl, and ethyl; $R^{20},\ R^{21},\ R^{23},\ R^{24},$ and $R^{15}\,are$ independently selected Qb is NR20R21 or C(NR25) NR23R24; Q* is CH1.

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fluoro, chloro, hydroxymethyl, carboxy, and cyano;

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95. The compound of claim 94 or a pharmaceutically acceptable salt thereof, wherein;

cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, oxalan-2-yl, 2-(2R)-bicyclo[2.2.1]-heptyl, oxetan-3-yl, B is selected from the group consisting of

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azetidin-1-yl, azetidin-2-yl, azetidin-3-yl, 1-

pyrrolidinyl and 1-piperidinyl;

X° is selected from the group consisting of hydrido, A is selected from the group consisting of a bond, CH, CH, CH, and CH, CH, CH,;

R¹ is selected from the group consisting of hydrido, hydroxy, amino, amidino, aminomethyl, cyano, methyl, trifluoromethyl, hydroxymethyl, and fluoro;

hydroxy, hydroxymethyl, amino, aminomethyl, cyano, methyl, trifluoromethyl, and fluoro;

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aminophenyl, 3-amino-5-(N-benzylamidocarbonyl)phenyl, 3amino-5-(N-(2-chlorobenzyl)amidocarbonyl)phenyl, 3-amino-(2-trifluoromethylbenzyl)amidocarbonyl)phenyl, 3-amino-5-(N-(1-phenylethyl)amidocarbonyl)phenyl, 3-amino-5-(N-(1-5-(N-(3-fluorobenzyl)amidocarbonyl)phenyl, 3-amino-5-(Nmethyl-1-phenylethyl) amidocarbonyl)phenyl, 3-amino-5-(N-R' is selected from the group consisting of 3amidocarbonyl-5-aminophenyl, 3-amidocarbonyl-5benzylamidosulfonyl)phenyl, 3-amino-5-(N-(2-

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chlorobenzyl)amidosulfonyl)phenyl, 3-amino-5-(Nisobutylamidocarbonyl)phenyl, 3-amino-5-(N-(2isopropylamidocarbonyl)phenyl, 3-amino-5-(Npropylamidocarbonyl) phenyl, 3-amino-5-(Nethylamidocarbonyl)phenyl, 3-amino-5-(N-

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cyclohexylamidocarbonyl)phenyl, 5-amino-2-fluorophenyl, cyclopentylamidocarbonyl)phenyl, 3-amino-5-{Ncyclobutylamidocarbonyl)phenyl, 3-amino-5-(Nbutyl)amidocarbonyl)phenyl, 3-amino-5-(N-

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carboxymethyl-5-hydroxyphenyl, 3-carboxymethylphenyl, 3methylphenyl, 5-amino-2-methylthiophenyl, 3-aminophenyl, 3-carboxyphenyl, 3-carboxy-5-aminophenyl, 3-carboxy-5methoxycarbonylphenyl, 3-amidinophenyl, 3-amino-2hydroxyphenyl, 3-carboxymethyl-5-aminophenyl, 3-3-amino-5-hydroxymethylphenyl, 5-amino-3-

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diaminophenyl, 3-dimethylaminophenyl, 2-fluorophenyl, 3-

chlorophenyl, 2-chlorophenyl, 3-cyanophenyl, 3,5-

fluorophenyl, 2.5-difluorophenyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 3-methanesulfonylaminophenyl, 2-methoxyphenyl, 3-methoxyphenyl, 3-methoxyaminophenyl, 3-methoxycarbonylphenyl, 2-methylaminophenyl, 3-methylphenyl, 4-methylphenyl, 3-methylphenyl, 3-trifluoroacetamidophenyl, 3-trifluoromethylphenyl, 2-trifluoromethylphenyl, 5-amino-2-thienyl, 5-amino-3-thienyl, 3-bromo-2-thienyl, 3-pyridyl, 4-pyridyl, 2-thienyl, and 3-thienyl;

 Y^o is selected from the group consisting of: $1-Q^b-4-Q^a-2-R^{16}-3-R^{19}-6-R^{19} benzene, \ 2-Q^b-5-Q^a-6-R^{17}-4-R^{18}-3-R^{19} pyridine, \ 3-Q^b-6-Q^a-2-R^{16}-5-R^{16}-4-R^{19} pyridine, \ 3-Q^b-5-Q^a-4-R^{16}-2-R^{16}-2-R^{16}-4-R^{17} thiophene; \ and \ 2-Q^b-5-Q^a-3-R^{16}-4-R^{17} thiophene; \$

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Ris and Ris are independently selected from the group consisting of hydrido, amidino, amino, aminomethyl, methoxy, methylamino, hydroxy, hydroxymethyl, fluoro, chloro, and cyano;

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R¹⁷ and R¹⁸ are independently selected from the group consisting of hydrido, fluoro, chloro, hydroxy, hydroxymethyl, amino, carboxy, and cyano;

Q^b 18 C (NR²⁵) NR²³R²⁴;

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R²³, R²⁴, and R²⁵ are independently hydrido or methyl; Q* is CH₂. 96. The compound of claim 95 or a pharmaceutically acceptable salt thereof, wherein;

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B is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, oxalan-2-yl, 2-(2R)-bicyclo[2.2.1]-heptyl, oxetan-3-yl, azetidin-1-yl, azetidin-2-yl, azetidin-3-yl, and 1-piperidinyl;

A is selected from the group consisting of a bond, ${\rm CH_3CH_2CH_2}$ and ${\rm CH_3CH_2CH_3}$

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X° is selected from the group consisting of hydrido, hydroxy, amino, amidino, aminomethyl, cyano, methyl, trifluoromethyl, hydroxymethyl, and fluoro;

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R¹ is selected from the group consisting of hydrido, hydroxy, hydroxymethyl, amino, aminomethyl, cyano, methyl, trifluoromethyl, and fluoro;

R' is selected from the group consisting of 3-amidocarbonyl-5-aminophenyl, 3-amino-5-(N-benzylamidocarbonyl)phenyl, 3-amino-5-(N-(2-chlorobenzyl)amidocarbonyl)phenyl, 3-amino-5-(N-(3-fluorobenzyl)amidocarbonyl)phenyl, 3-amino-5-(N-(2-trifluoromethylbenzyl)amidocarbonyl)phenyl, 3-amino-5-(N-(1-phenylethyl)amidocarbonyl)phenyl, 3-amino-5-(N-(1-phenylethyl)amidocarbonyl)phenyl

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(1-phenyletnyl amidocarbonyl)phenyl, 3-amino-5 (N-(1-methyl-1-phenylethyl)amidocarbonyl)phenyl, 3-amino-5 (N-(2-benzylamidosulfonyl)phenyl, 3-amino-5 (N-(2-chlorobenzyl)amidosulfonyl)phenyl, 3-amino-5 (N-ethylamidocarbonyl)phenyl, 3-amino-5 (N-fsopropylamidocarbonyl)phenyl, 3-amino-5 (N-fsobutylamidocarbonyl)phenyl, 3-amino-5 (N-fsobutylamidocarbonyl)phenyl, 3-amino-5 (N-cyclobutylamidocarbonyl)phenyl, 3-amino-5 (N-cyclobutylamidocarbonyl)phenyl

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cyclopentylamidocarbonyl)phenyl, 3-amino-5-(N-cyclohexylamidocarbonyl)phenyl, 3-aminophenyl, 3-carboxy 5-aminophenyl, 3-chlorophenyl, 3,5-diaminophenyl, 3-dimethylaminophenyl, 3-hydroxyphenyl, 3-methanesulfonylaminophenyl, 3-methylphenyl, 3-methylphenyl, 3-methylphenyl, 3-methylphenyl, 3-

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trifluoroacetamidophenyl, 3-bromo-2-thienyl, 2-thienyl,
and 3-thienyl;
 yº is selected from the group consisting of 5amidino-2-thienylmethyl, 4-amidinobenzyl, 2-fluoro-4-

97. The compound of claim 90 wherein the compound is selected from the group consisting of:

amidinobenzyl, and 3-fluoro-4-amdinobenzyl.

or a pharmaceutically acceptable salt thereof, wherein; R' is 3-aminophenyl, B is cyclopropyl, A is a bond Y° is 4-amidinobenzyl, and R¹ is chloro;

 R^2 is 3-aminophenyl, B is cyclobutyl, A is a bond, Y°

is 4-amidino-2-fluorobenzyl, and R' is chloro;

 R^2 is 3-aminopheny1, B is cyclobuty1, A is a bond, Y^{o} is 4-amidinobenzyl, and R' is chloro;

R2 is 3-aminophenyl, B is cyclopropyl, A is a bond,

 Y° is 4-amidino-2-fluorobenzyl, and R^{1} is chloro;

 R^2 is 3-aminophenyl, B is cyclobutyl, A is a bond, $Y^{\rm o}$ is 4-amidinobenzyl, and R1 is hydrido;

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 R^2 is 3-aminophenyl, B is cyclobutyl, A is a bond, Y^{o} is 4-amidino-3-fluorobenzyl, and R¹ is chloro;

R' is 3-aminophenyl, B is cyclopentyl, A is a bond,

R2 is 5-amino-2-thienyl, B is cyclobutyl, A is a Y° is 4-amidinobenzyl, and R¹ is chloro;

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 R^2 is 3-aminophenyl, B is cyclopropyl, A is $CH_2,\ Y^0$ is bond, Y° is 4-amidinobenzyl, and R¹ is chloro; 4-amidinobenzyl, and R1 is chloro;

R² is 3-aminophenyl, B is 2-(2R)-bicyclo[2.2.1]heptyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is

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R2 is 3-aminophenyl, B is cyclopentyl, A is a bond,

R² is 3-aminophenyl, B is cyclohexyl, A is CH₂CH₂, Y⁰ Yº is 4-amidino-2-fluorobenzyl, and R¹ is chloro; is 4-amidinobenzyl, and R1 is hydrido;

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R² is 3-aminophenyl, B is oxalan-2-yl, A is CH, Y 18 4-amidinobenzyl, and R1 is chloro;

R' is 3-aminophenyl, B is 1-piperidinyl, A is CH, CH, Yo is 4-amidinobenzyl, and R1 is chloro,

R2 is 3-aminophenyl, B is 1-pyrrolidinyl, A is CH,CH,CH, Y is 4-amidinobenzyl, and R' is chloro;

R' is 3-amino-5-carboxyphenyl, B is cyclobutyl, A is R² is 3-amino-5-carbomethoxyphenyl, B is cyclobutyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is hydrido;

R' is 3,5-diaminophenyl, B is cyclobutyl, A is a a bond, Y° is 4-amidinobenzyl, and R¹ is hydrido; bond, Y° is 4-amidinobenzyl, and R¹ is hydrido;

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R' is 2-amino-6-carboxy-4-pyridyl, B is cyclobutyl, A is a bond, Y^0 is 4-amidinobenzyl, and R^1 is hydrido;

R² is 3-amino-5-carbomethoxyphenyl, B is cyclobutyl, A is a bond, Y^o is 4-amidinobenzyl, and R^1 is chloro;

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R² is 3-amino-5-carboxyphenyl, B is cyclobutyl, A is

R' is 3,5-diaminophenyl, B is cyclopropyl, A is a a bond, Y^0 is 4-amidinobenzyl, and R^1 is chloro,

R' is 3,5-diaminophenyl, B is cyclobutyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

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bond, Y° is 4-amidino-2-fluorobenzyl, and R¹ is chloro; R2 is 3,5-diaminophenyl, B is cyclopropyl, A is a

bond, Y° is 4-amidino-2-fluorobenzyl, and R¹ is chloro; R² is 3,5-diaminophenyl, B is cyclobutyl, A is a bond, Y° is 4-amidinobenzyl, and R' is hydrido;

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bond, Y° is 4-amidino-3-fluorobenzyl, and R¹ is chloro; R² is 3,5-diaminophenyl, B is cyclobutyl, A is a

R2 is 3-carboxy-5-aminophenyl, B is cyclopropyl, A is R' is 3,5-diaminophenyl, B is cyclopentyl, A is a bond, Yo is 4-amidinobenzyl, and R1 is chloro;

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is 3-carboxy-5-aminophenyl, B is cyclopropyl, A is is 3-carboxy-5-aminophenyl, B is cyclobutyl, A is a bond, Υ^{o} is 4-amidino-2-fluorobenzyl, and R^{1} is chloro; <u>ب</u> ъ

a bond, Y° is 4-amidinobenzyl, and R¹ is chloro;

a bond, Y° is 4-amidino-2-fluorobenzyl, and R¹ is chloro,

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a bond, Y' is 4-amidinobenzyl, and R' is hydrido;

a bond, Y' is 4-amidinobenzyl, and R' is hydrido;

a ' i - 1 control - aminonbown B is cyclobutyl B is

R' is 3-carboxy-5-aminophenyl, B is cyclobutyl, A is a bond, Y' is 4-amidino-3-fluorobenzyl, and R' is chloro; R' is 3-carboxy-5-aminophenyl, B is cyclopentyl, A is a bond, Y' is 4-amidinobenzyl, and R' is chloro;

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 R^2 is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is cyclopropyl, A is a bond, Y° is 4-amidinobenzyl, and R^{i} is chloro;

 R^2 is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is cyclobutyl, A is a bond, Y° is/4-amidino-2-fluorobenzyl, and R^1 is chloro;

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 R^2 is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is cyclobutyl, A is a bond, Y^{α} is 4-amidinobenzyl, and R^1 is chloro;

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 R^2 is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is cyclopropyl, A is a bond, Y° is 4-amidino-2-fluorobenzyl, and R¹ is chloro;

 R^2 is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is cyclobutyl, A is a bond, Y° is 4-amidinobenzyl, and R^1 is hydrido;

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 R^2 is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is cyclobutyl, A is a bond, Y^{o} is 4-amidino-3-fluorobenzyl, and R^1 is chloro;

 R^2 is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is cyclopentyl, A is a bond, $Y^{\rm 0}$ is 4-amidinobenzyl, and $R^{\rm 1}$ is chloro;

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R² is 3-amino-5-(N-(2-

chlorobenzyl)amidosulfonyl)phenyl, B is cyclopropyl, A is a bond, Y^o is 4-amidinobenzyl, and R^1 is chloro; R^2 is 3-amino-5-(N-(2-

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chlorobenzyl) amidosulfonyl) phenyl, B is cyclobutyl, A is a bond, Y⁰ is 4-amidino-2-fluorobenzyl, and R¹ is chloro; R² is 3-amino-5-(N-(2-

chlorobenzyl)amidosulfonyl)phenyl, B is cyclobutyl, A is a bond, Y° is 4-amidinobenzyl, and R^{1} is chloro;

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R² is 3-amino-5-(N-(2-

chlorobenzyl)amidosulfonyl)phenyl, B is cyclopropyl, A is a bond, Y^o is 4-amidino-2-fluorobenzyl, and R^1 is chloro, R^2 is 3-amino-5- $(N-\{2-$

chlorobenzyl)amidosulfonyl)phenyl, B is cyclobutyl, A is a bond, Y° is 4-amidinobenzyl, and R' is hydrido;

R² is 3-amino-5-(N-(2-chlorobenzyl)amidosulfonyl)phenyl, B is cyclobutyl, A is a bond, Y° is 4-amidino-3-fluorobenzyl, and R¹ is chloro;

 R^2 is 3-amino-5-(N-(2-chlorobenzyl) amidosulfonyl)phenyl, B is cyclopentyl, A is a bond, γ^o is 4-amidinobenzyl, and R^1 is chloro;

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R² is 3-amino-5-(N-(2-

trifluoromethylbenzyl)amidocarbonyl)-phenyl, B is

cyclopropyl, A is a bond, Y' is 4-amidinobenzyl, and R' is
chloro;

R² is 3-amino-5-(N-(2-

trifluoromethylbenzyl)amidocarbonyl)-phenyl, B is cyclobutyl, A is a bond, Y° is 4-amidino-2-fluorobenzyl, and R¹ is chloro;
R² is 3-amino-5-(N-(2-trifluoromethylbenzyl) amidocarbonyl)-phenyl, B is cyclobutyl, A is a bond, Y° is 4-amidinobenzyl, and R¹ is

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R² is 3-amino-5-(N-(2-trifluoromethylbenzyl)amidocarbonyl)-phenyl, B is cyclopropyl, A is a bond, Y^o is 4-amidino-2-fluorobenzyl, and R¹ is chloro;

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R² is 3-amino-5-(N-(2-30 trifluoromethylbenzyl)amidocarbonyl)-phenyl, B is cyclobutyl, A is a bond, Y° is 4-amidinobenzyl, and R² is hydrido;

R² is 3-amino-5-(N-(2trifluoromethylbenzyl)amidocarbonyl).phenyl, B is
cyclobutyl; A is a bond, Yº is 4-amidino-3-fluorobenzyl,
and R¹ is chloro;

R2 is 3-amino-5-(N-(2-

cyclopentyl, A is a bond, Y^{0} is 4-amidinobenzyl, and R^{1} is trifluoromethylbenzyl)amidocarbonyl)-phenyl, B is chloro.

The compound of claim 67 having the structure: 98.

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or a pharmaceutically acceptable salt thereof, wherein;

M is N or N→O;

B is selected from the group consisting of:

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substituted by R15, and any carbon adjacent to both R11 and substituted by R13, a carbon adjacent to R16 and two atoms from the carbon at the point of attachment is optionally substituted by R16, a carbon adjacent to R12 and two atoms from the carbon at the point of attachment is optionally (i) phenyl or a heteroaryl of 5 or 6 ring members, optionally substituted by R12, the other carbon adjacent wherein a carbon adjacent to the carbon at the point of to the carbon at the point of attachment is optionally attachment of said phenyl or heteroaryl ring to A is R15 is optionally substituted by R14;

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of the group consisting of R12, R11, R14, R15, and R16; and haloalkyl, wherein each member of group B is optionally from the point of attachment of B to A with one or more substituted at any carbon up to and including 6 atoms (ii) hydrido, trialkylsilyl, C2-C8 alkyl, C3-C8 alkylenyl, C3-C8 alkenyl, C3-C8 alkynyl, and C2-C8

optionally substituted with R¹³, a ring carbon other than the ring carbon at the point of attachment of B to A is saturated heterocyclyl, wherein each ring carbon is C3-C12 cycloalkyl or a C4-C9

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adjacent to the R12 position is optionally substituted with atoms from the point of attachment and adjacent to the R^{10} position is optionally substituted with R11, a ring carbon or nitrogen three atoms from the point of attachment and time, ring carbons and a nitrogen adjacent to the carbon of attachment is optionally substituted with R^{10} , a ring adjacent to the R' position and two atoms from the point carbon or nitrogen adjacent to the R13 position and two R33, and a ring carbon or nitrogen four atoms from the than one ring carbon is substituted by oxo at the same optionally substituted with oxo provided that no more substituted with R12, a ring carbon or nitrogen three substituted with R' or R'3, a ring carbon or nitrogen point of attachment and adjacent to the \mathbb{R}^{11} and \mathbb{R}^{13} atoms from the point of attachment is optionally atom at the point of attachment are optionally positions is optionally substituted with R14;

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alkoxyamino, haloalkanoyl, nitro, alkylamino, alkylthio, R12, R11, R14, R15, and R16 are independently selected aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, alkylsulfonamido, amidosulfonyl, alkyl, haloalkylthio, alkanoyloxy, alkoxy, hydroxy, amino, alkenyl, halo, haloalkyl, haloalkenyl, haloalkoxy, haloacetamido, amidino, guanidino, alkylenedioxy, from the group consisting of hydrido, acetamido, hydroxyalkyl, alkylamino, carboalkoxy, carboxy, carboxamido, cyano, and Q^b;

amidino, guanidino, alkylenedioxy, haloalkylthio, alkoxy, heterocyclylalkoxy, hydroxy, amino, alkylamino, N-alkyl-R, R10, R11, R12, and R11 are independently selected N-arylamino, arylamino, aralkylamino, heteroarylamino, haloacetamido, alkoxyamino, alkanoyl, haloalkanoyl, cycloalkoxy, cycloalkylalkoxy, aralkoxy, aryloxy, from the group consisting of hydrido, acetamido, neteroaryloxy, heteroaralkoxy,heterocyclyloxy, heteroaralkylamino, heterocyclylamino,

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heteroarylBulfonyl, amidosulfonyl, alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, hydroxyhaloalkyl, aminoalkyl, carboalkoxy, carboxy, heteroarylsulfinyl, alkylsulfamido, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, cycloalkylsulfonyl, arylsulfinyl, aralkylsulfinyl, cycloalkylsulfinyl, heterocyclylalkylamino, alkylthio, alkylsulfinyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, carboxyalkyl, carboxamido, and cyano;

A is a bond or $(CH(R^{15}))_{pa}$ - $(W^{7})_{rr}$ wherein rr is 0 or 1, pa is an integer selected from 0 through 3, and W' is selected from the group consisting of 0, S, C(0), (R')NC(O), (R')NC(S), and N(R');

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R' is selected from the group consisting of hydrido,

R15 is selected from the group consisting of hydrido, hydroxy, halo, alkyl, and haloalkyl; hydroxy and alkyl;

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Ja is Nor C-X°;

Jb is N or C-R1;

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hydroxy, hydroxyamino, alkoxy, hydroxyalkyl, alkoxyamino, R¹ and X° are independently selected from the group consisting of hydrido, alkyl, cyano, halo, haloalkyl, haloalkoxy, amino, aminoalkyl, alkylamino, amidino, thiol, and alkylthio;

R2 is Z0-Q;

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Z° is selected from the group consisting of:

independently selected from 0 through 3 and W° is selected from the group consisting of 0, S, C(0), S.(0), $N(R^{43})$, and a bond, (CR41R42), wherein q is 1 or 2, and $(CH(R^{41}))_g-W^0-(CH(R^{42}))_p$ wherein g and p are integers ON (R41); and

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independently 0 or 1 and W22 is selected from the group consisting of CR"=CR", 1,2-cyclopropyl, 1,2-cyclobutyl 1,2-cyclohexyl, 1,3-cyclohexyl, 1,2-cyclopentyl, 1,3-(11) (CH(R41)),-W22-(CH(R42)), wherein e and h are cyclopentyl, 2,3-morpholinyl, 2,4-morpholinyl, 2,6-

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pyridine ring and W^{22} is optionally substituted with one or more substituents selected from the group consisting of selected from the group consisting of hydrido, hydroxy, tetrahydrofuranyl, wherein 2° is directly bonded to the pyrrolidinyl, 2,4-pyrrolidinyl, 2,5-pyrrolidinyl, 3,4piperidinyl, 1,2-pyrrolidinyl,1,3-pyrrolidinyl, 2,3-R9, R10, R11, R12, and R13; R41 and R42 are independently piperidinyl, 2,4-piperidinyl, 2,6-piperidinyl, 3,4morpholinyl, 3,4-morpholinyl, 3,5-morpholinyl, 1,2piperazinyl, 1,3-piperazinyl, 2,3-piperazinyl, 2,6piperazinyl, 1,2-piperidinyl, 1,3-piperidinyl, 2,3tetrahydrofuranyl, 2,5-tetrahydrofuranyl, and 3,4pyrrolidinyl, 2,3-tetrahydrofuranyl, 2,4-

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(i) phenyl or a heteroaryl of 5 or 6 ring members, Q is selected from the group consisting of: alkyl, and amino;

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optionally substituted by R3, the other carbon adjacent to substituted by R13, and any carbon adjacent to both R10 and R¹² is optionally substituted by R¹¹, with the proviso that substituted by R10, a carbon adjacent to R13 and two atoms from the carbon at the point of attachment is optionally from the carbon at the point of attachment is optionally substituted by R13, a carbon adjacent to R9 and two atoms wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to \mathbf{Z}^o is the carbon at the point of attachment is optionally Q is other than a phenyl when Z' is a bond; and

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(11) hydrido with the proviso that Zº is selected from other than a bond;

consisting of hydrido, hydroxyalkyl, alkyl, alkoxyalkyl, K is CHR" wherein R" is selected from the group alkylthioalkyl, and haloalkyl;

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E' is selected from the group consisting of a bond C(0)N(H), (H)NC(O), (R')NS(O), and S(O),N(R');

YAT 18 Qb-Q";

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Q* is (CR37R34), wherein b is an integer selected from

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I through 4, R³⁷ is selected from the group consisting of hydrido, alkyl, and haloalkyl, and R³⁸ is selected from the group consisting of hydrido, alkyl, haloalkyl, aroyl, and heteroaroyl with the proviso that there is at least one aroyl or heteroaroyl substituent, with the further proviso that no more than one aroyl or heteroaroyl is bonded to (CR³?R³⁸), at the same time, with the still further proviso that said aroyl and said heteroaroyl are optionally substituted with one or more substituents selected from the group consisting of R¹⁸, R¹⁷, R¹⁸, and R¹⁸, with another further proviso that said aroyl and said heteroaroyl are bonded to the CR³?R³⁸ that is directly

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than the one bonding said aroyl or said heteroaroyl; R¹¹ and R¹ª are independently selected from the group consisting of hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkoxyamino, alkylamino, alkylsulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano;

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more than one alkyl or one haloalkyl is bonded to a CR11R1

at the same time, and with the additional proviso that

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said alkyl and haloalkyl are bonded to a carbon other

bonded to E', with still another further provise that no

Ris or Ris are selected from the group consisting of:

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(1) hydrido, amidino, guanidino, carboxy, haloalkylthio, alkoxy, hydroxy, amino, alkoxyamino, alkylamino, alkylthio, alkylaulfinyl, alkylsulfonyl, alkanoyl, haloalkanoyl, alkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, aminoalkyl, and cyano; and

inalogikoky, hydroxyanyi, aminoanyi, and cynno, and (ii) NR²⁰R²¹, N(R²⁰)C(NR²³)N(R²³) (R²³) (R²³), and C (NR²³)NR²³R²⁴, with the proviso that R¹⁶, R¹⁹, and Q² are not simultaneously hydrido;

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 Q^b is selected from the group consisting of $NR^{28}r_1^{14}$, hydrido, $N(R^{26})C(NR^{25})N(R^{23})$ (R^{24}), and $C(NR^{25})NR^{23}R^{24}$, with the proviso that no more than one of R^{20} and R^{21} is selected from the group consisting of hydroxy, amino, alkylamino,

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and dialkylamino at the same time and with the further proviso that no more than one of R²³ and R²⁴ is selected from the group consisting of hydroxy, amino, alkylamino, and dialkylamino at the same time;

R²⁰, R²¹, R²¹, R²³, and R²⁶ are independently selected from the group consisting of hydrido, alkyl, hydroxy, amino, alkylamino and dialkylamino.

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99. The compound of claim 98 having the structure

or a pharmaceutically acceptable salt thereof, wherein; M is N or N \rightarrow O;

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B is selected from the group consisting of:

(1) phenyl, 2-thienyl, 3-thienyl, 2-furyl, 3-furyl,
2-pyrrolyl, 3-pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-byrazolyl, 2-thiazolyl, 3-soxazolyl, and 5-

pyrazolyl, 4-pyrazolyl, 2-imidzolyl, 1-imidzolyl, 3-imoxazolyl, and 5-imoxazolyl, 4-pyrazolyl, 2-thiazolyl, 3-isoxazolyl, and 5-isoxazolyl, wherein a carbon adjacent to the carbon at the point of attachment of said phenyl or heteroaryl ring to A is optionally substituted by R¹³, the other carbon adjacent to the carbon at the point of attachment is optionally substituted by R¹⁴, a carbon adjacent to R¹³ and two atoms from the carbon at the point of attachment is optionally substituted by R¹³, a carbon adjacent to R¹⁴ and two atoms from the carbon at the point of attachment is optionally substituted by R¹³, and any carbon adjacent to both R¹³ and R¹⁵ is optionally substituted by R¹⁴;

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(ii) hydrido, ethyl, 2-propenyl, 2-propynyl, propyl,
isopropyl, butyl, 2-butenyl, 2-butynyl, sec-butyl, tertbutyl, isobutyl, 2-methylpropenyl, 1-pentyl, 2-pentenyl,
3-pentenyl, 2-pentynyl, 3-pentynyl, 2-pentyl, 3-pentyl,

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butenyl, 1-heptyl, 2-heptenyl, 3-heptenyl, 4-heptenyl, 5neptenyl, 2-heptynyl, 3-heptynyl, 4-heptynyl, 5-heptynyl, nethyl-4-hexenyl, 1-methyl-2-hexynyl, 1-methyl-3-hexynyl, hexenyl, 2-hexynyl, 3-hexynyl, 4-hexynyl, 2-hexyl, 1-2-heptyl, 1-methyl-2-hexenyl, 1-methyl-3-hexenyl, 1-2-methylbutyl, 2-methyl-2-butenyl, 3-methylbutyl, 3-.-methyl-4-hexynyl, 3-heptyl, 1-ethyl-2-pentenyl, 1methyl-2-butenyl, 1-hexyl, 2-hexenyl, 3-hexenyl, 4methyl-2-pentenyl, 1-methyl-3-pentenyl, 1-methyl-2pentynyl, 1-methyl-3-pentynyl, 3-hexyl, 1-ethyl-2-

ethyl-3-pentenyl, 1-ethyl-2-pentynyl, 1-ethyl-3-pentynyl, 3,3,3-trifluoropropyl, wherein each member of group B is optionally substituted at any carbon up to and including 5 atoms from the point of attachment of B to A with one or more of the group consisting of R12, R13, R14, R15, and trifluoromethylpentyl, 5,5,6,6.pentafluorohexyl, and ,2,2-trifluoroethyl, 2,2-difluoropropyl, 4crifluoromethyl-5,5,5-trifluoropentyl, 4-R³6; and

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substituted with R¹³, ring carbons and a nitrogen adjacent cetrahydrothienyl, wherein each ring carbon is optionally cyclopropyl, cyclobutyl, cyclopentyl, piperazinyl, 2-piperazinyl, 1-piperidinyl, 2-piperidinyl, azetidin-2-yl, azetidin-3-yl, bicyclo[3.1.0]hexan-6-yl, nitrogen adjacent to the R' position and two atoms from the point of attachment is optionally substituted with optionally substituted with R° or R13, a ring carbon or bicyclo[2.2.1]-heptyl, oxetan-3-yl, azetidin-1-yl, to the carbon atom at the point of attachment are 9-piperidinyl, 4-piperidinyl, 1-pyrrolidinyl, 2-2-morpholinyl, 3-morpholinyl, 4-morpholinyl, 1tetrahydropyranyl, 2-tetrahydrothienyl, and 3cyclohexyl, cycloheptyl, oxalan-2-yl, 2-(2R)cyrrolidinyl, 3-pyrrolidinyl, 2-dioxanyl, 2tetrahydrofuranyl, 3-tetrahydrofuranyl, 2cetrahydropyranyl, 3-tetrahydropyranyl, 4-

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position and two atoms from the point of attachment is $R^{10},\ \mbox{and}\ \mbox{a ring carbon or nitrogen adjacent to the }R^{13}$ optionally substituted with R12;

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from the group consisting of hydrido, amidino, guanidino, trifluoroethyl, fluoro, chloro, bromo, amidosulfonyl, N-R12, R13, R14, R15, and R16 are independently selected methylamino, dimethylamino, methoxyamino, methylthlo, ethylthio, trifluoromethyl, pentafluoroethyl, 2,2,2methylamidosulfonyl, hydroxymethyl, amidocarbonyl, methyl, ethyl, methoxy, ethoxy, hydroxy, amino, Ncarboxy, cyano, and Qb;

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ethoxy, hydroxy, amino, N-methylamino, N,N-dimethylamino, trifluoroethyl, fluoro, chloro, bromo, amidosulfonyl, N-R, R11, and R11 are independently selected from the methylthio, trifluoromethyl, pentafluoroethyl, 2,2,2group consisting of hydrido, methyl, ethyl, methoxy, hydroxymethyl, 1-hydroxyethyl, amidocarbonyl, Nmethylamidosulfonyl, N,N-dimethylamidosulfonyl, methylamidocarbonyl, carboxy, and cyano;

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R10 and R12 are independently selected from the group consisting of hydrido, amidino, amidocarbonyl, Nmethylamidocarbonyl, N-benzylamidocarbonyl, N-(2chlorobenzyl) amidocarbonyl, N-(3-

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trifluoromethylbenzyl)amidocarbonyl, N-(1fluorobenzyl) amidocarbonyl, N-(2-

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N- (2-2-hydroxyethyl, carboxy, carboxymethyl, amino, acetamido, methoxy, ethoxy, hydroxy, hydroxymethyl, 1-hydroxyethyl, cyclobutylamidocarbonyl, N-cyclopentylamidocarbonyl, Ntrifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, chlorobenzyl)amidosulfonyl, N-ethylamidocarbonyl, Nisobutylamidocarbonyl, N-(2-butyl)amidocarbohyl, Nphenylethyl) amidocarbonyl, N-benzylamidosulfonyl, cyclohexylamidocarbonyl, guanidino, methyl, ethyl, isopropylamidocarbonyl, N-propylamidocarbonyl, Ntrifluoroacetamido, aminomethyl, N-methylamino, phenylethyl)amidocarbonyl, N-(1-methyl-1-

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methanesulfonamido, methoxycarbonyl, fluoro, chloro, methylamidosulfonyl, N,N-dimethylamidosulfonyl, dimethylamino, methoxyamino, amidosulfonyl, Nbromo, and cyano; A is selected from the group consisting of a bond, NH, N(CH3), CH2, CH3CH, CH3CH2, and CH2CH2CH2;

Ja is N or C-X';

Jb is N or C-R1;

aminomethyl, methylamino, cyano, methyl, trifluoromethyl, R' and X° are independently selected from the group consisting of hydrido, hydroxy, hydroxymethyl, amino, methoxy, methylthio, trifluoromethoxy, fluoro, and

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is optionally substituted by R^{10} , a carbon adjacent to R^{13} is optionally substituted by R^{12} , and any carbon adjacent carbon adjacent to the carbon at the point of attachment is optionally substituted by R^{13} , a carbon adjacent to R^{9} and two atoms from the carbon at the point of attachment and two atoms from the carbon at the point of attachment pyridine ring is optionally substituted by R°, the other wherein a carbon adjacent to the carbon at the point of R' is selected from the group consisting of phenyl, attachment of said phenyl or heteroaryl ring to the thiazoly1, 3-isoxazoly1, 2-pyridy1, and 3-pyridy1, to both R10 and R12 is optionally substituted by R11; 2-thienyl, 2-furyl, 2-pyrrolyl, 2-imidazolyl, 2-

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Q* is selected from the group consisting of: YM is Qb-Q";

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 $C[R^{37}(benzoy1) (CR^{37}R^{38})_b]$, $C[R^{37}(2-pyridylcarbony1) (CR^{37}R^{38})_b]$,

C[R17 (3-pyridylcarbonyl) (CR17R18) b], C[R37 (4thiazolylcarbonyl)(CR37R18)b], C[R17(4thienylcarbonyl) (CR37R38) b], C[R37(3thienylcarbonyl) $(CR^{17}R^{18})_{b}$], $C[R^{37}(2$ pyridylcarbonyl) (CR37R38), C[R37(2-

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thiazolylcarbonyl) ($(CR^{17}R^{16})_{b}$), wherein b is an integer thiazolylcarbonyl) $(CR^{17}R^{18})_{b}$], and $C[R^{17}(5-$

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(amidocarbonymethylene) group, and with the still further heteroaroyls are optionally substituted with one or more selected from the group consisting of hydrido, alkyl, and of the benzoyl or heteroarcyl, with the further proviso that said benzoyl or said heteroaroyl are bonded to the than the meta and para carbons relative to the carbonyl proviso that is no more than one alkyl or one haloalkyl selected from 1 through 3, R3 and R30 are independently haloalkyl, with the proviso that said benzoyl and the substituents selected from the group consisting of R^{16} , optionally substituted at a carbon selected from other R17, R18, and R19 with the proviso that R17 and R18 are carbon directly bonded to amide nitrogen of the 1is bonded to a CR17R18 at the same time;

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pentafluoroethyl, 2,2,2-trifluoroethyl, trifluoromethoxy, R^{16} , R^{17} , R^{18} , and R^{19} are independently selected from the group consisting of hydrido, methyl, ethyl, amidino, aminoethyl, 2-aminoethyl, N-methylamino, dimethylamino, guanidino, methoxy, hydroxy, amino, aminomethyl, 1methylsulfinyl, methylsulfonyl, trifluoromethyl, methylthio, ethylthio, trifluoromethylthio,

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R23, R24, R25, and R26 are independently selected from Q^b is $C(NR^{25})NR^{23}R^{24}$ or $N(R^{24})C(NR^{25})N(R^{21})$ (R^{24}); and the group consisting of hydrido, methyl, and ethyl. fluoro, chloro, hydroxymethyl, carboxy, and cyano;

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pharmaceutically acceptable salt thereof, wherein; The compound of claim 99 or a M 18 N-O;

B is selected from the group consisting of:

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methoxyaminophenyl, 3-methoxyphenyl, 4-methoxyphenyl, 3-(1) 2-aminophenyl, 3-aminophenyl, 3-amidinophenyl, dichlorophenyl, 2-fluorophenyl, 3-fluorophenyl, 3,4difluorophenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 3hydroxyphenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-4-amidinophenyl, 3-carboxyphenyl, 3-carboxy-5-

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methylphenyl, 4-methylphenyl, phenyl, 3trifluoromethylphenyl, 2-imidazoyl, 2-pyridyl, 3-pyridyl,
5-chloro-3-trifluoromethyl-2-pyridyl, 4-pyridyl, 2thienyl, 3-thienyl, and 3-trifluoromethyl-2-pyridyl;

(ii) hydrido, ethyl, 2-propenyl, 2-propynyl, isopropyl, butyl, 2-butyl, (R)-2-butyl, (S)-2-butyl, tert-butyl, isobutyl, 1-pentyl, 3-pentyl, 2-methylbutyl, 2,2,2-trifluoroethyl, 6-amidocarbonylhexyl, 4-methyl-2-pentyl, 3-hydroxypropyl, 1-methoxy-2-propyl, 2-methyl-2-butyl, 2-dimethylaminopropyl, 1-cyanoethyl, 6-hydroxyhexyl, 2-hydroxyethyl, 2-amidinoethyl, 2-guanidinoethyl, 3-guanidinopropyl, 4-guanidinobutyl, 3-hydroxypropyl, 4-methylbutyl, 3-methylbutyl, 2-methylbutyl, (S)-2-methylbutyl, 3-methylbutyl, 3-methylbutyl, 3-methylbutyl, 3-methylbutyl, 3-methylbutyl, and 4-aminobutyl; and

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(111) cyclopropyl, cyclobutyl, cyclopentyl,
cyclohexyl, oxalan-2-yl, 2-(2R)-bicyclo[2.2.1]-heptyl,
oxetan-3-yl, azetidin-1-yl, azetidin-2-yl, azetidin-3-yl,
1-pyrrolidinyl and 1-piperidinyl;

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A is selected from the group consisting of a bond, CH, CH,CH, CH,CH,CH,CH,;

Ja is N or C-X°;

Jb is N or C-R1;

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R¹ and X° are independently selected from the group consisting of hydrido, hydroxy, hydroxymethyl, amino, aminomethyl, cyano, methyl, trifluoromethyl, fluoro, and chloro:

R² is selected from the group consisting of 3-amidocarbonyl-5-aminophenyl, 3-amidocarbonyl-5-aminophenyl, 3-amidocarbonyl) phenyl, 3-amino-5-(N-(2-chlorobenzyl) amidocarbonyl) phenyl, 3-amino-5-(N-(3-fluorobenzyl) amidocarbonyl) phenyl, 3-amino-6-(N-(2-trifluoromethylbenzyl) amidocarbonyl) phenyl, 3-amino-5-(N-(1-phenylethyl) amidocarbonyl) phenyl, 3-amino-5-(N-methyl-1-phenylethyl) amidocarbonyl) phenyl, 3-amino-5-(N-methyl-1-phenylethyl)

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benzylamidosulfonyl)phenyl, 3-amino-5-(N-(2-chlorobenzyl)amidosulfonyl)phenyl, 3-amino-5-(N-ethylamidocarbonyl)phenyl, 3-amino-5-(N-isopropylamidocarbonyl)phenyl, 3-amino-5-(N-isobutylamidocarbonyl)phenyl, 3-amino-5-(N-cisobutylamidocarbonyl)phenyl, 3-amino-5-(N-cyclobutylamidocarbonyl)phenyl, 3-amino-5-(N-cyclobutylamidocarbonyl)phenyl, 3-amino-5-(N-cyclobutylamidocarbonyl)phenyl, 3-amino-5-(N-cyclobexylamidocarbonyl)phenyl, 3-amino-2-fluorophenyl, 3-amino-2-fluorophenyl, 3-amino-2-fluorophenyl, 3-amino-2-methylphenyl, 3-amino-2-methylphenyl, 3-amino-2-methylphenyl, 3-aminophenyl, 3-aminophenyl, 3-aminophenyl, 3-carboxyp-5-hydroxyphenyl, 3-carboxymethyl-5-aminophenyl, 3-

methoxycarbonylphenyl, 3-amidinophenyl, 3-amino-2-methylphenyl, 5-amino-2-methylthiophenyl, 3-aminophenyl, 3-carboxyphenyl, 3-carboxy-5-aminophenyl, 3-carboxyphenyl, 3-carboxymethyl-5-aminophenyl, 3-carboxymethyl-5-hydroxyphenyl, 3-carboxymethylphenyl, 3-carboxymethylphenyl, 2-chlorophenyl, 3-cyanophenyl, 5-diaminophenyl, 2-fluorophenyl, 3-fluorophenyl, 2,5-difluorophenyl, 3-fluorophenyl, 3-fluo

hydroxyphenyl, 3-methanesulfonylaminophenyl, 2-methoxyphenyl, 3-methoxyphenyl, 3-methoxyphenyl, 3-methoxycarbonylphenyl, 2-methylaminophenyl, 3-methylphenyl, 3-methylphenyl, 3-methylphenyl, 3-trifluoroacetamidophenyl, 3-trifluoromethylphenyl, 2-trifluoromethylphenyl, 5-amino-2-thienyl, 3-bromo-2-thienyl, 3-thienyl, 3-bromo-2-thienyl, 3-thienyl, 3-thi

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Q* is selected from the group consisting of: [CH(benzoyl)](CH₂)_b, [CH(2-pyridylcarbonyl)](CH₂)_b, [CH(3-pyridylcarbonyl)](CH₂)_b, [CH(4pyridylcarbonyl)](CH₂)_b, [CH(2thienylcarbonyl)](CH₃)_b, [CH(3-thienylcarbonyl)](CH₃)_b,

pyridyl, 4-pyridyl, 2-thienyl, and 3-thienyl;

YAT 18 Qb-Q";

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thiazolylcarbonyl)](CH₂)_b, and [CH(5-thiazolylcarbonyl)](CH₃)_b, wherein b is an integer

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[CH(2-thiazolylcarbonyl)](CH2), [CH(4-

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R17 and R18 are optionally substituted at a carbon selected said benzoyl or said heteroarcyl are bonded to the carbon from other than the meta and para carbons relative to the benzoyl and said heteroaroyls are optionally substituted consisting of R^{16} , R^{17} , R^{18} , and R^{19} with the proviso that with one or more substituents selected from the group selected from 1 through 3, with the proviso that said carbonyl of the benzoyl or the heteroaroyl, and that directly bonded to amide nitrogen of the 1-

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 R^{16} and R^{19} are independently selected from the group methoxy, methylamino, hydroxy, hydroxymethyl, fluoro, consisting of hydrido, amidino, amino, aminomethyl, chloro, and cyano;

(amidocarbonymethylene) group;

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 \mathbb{R}^{17} and \mathbb{R}^{19} are independently selected from the group consisting of hydrido, fluoro, chloro, hydroxy, hydroxymethyl, amino, carboxy, and cyano;

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Qb is N(R26)C(NR25)N(R23)(R24);

 $R^{23},\ R^{24},\ R^{25},\ and\ R^{26}\,are$ independently hydrido or

methyl.

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101. The compound of claim 100 or a pharmaceutically acceptable salt thereof, wherein;

M is N→O;

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B is selected from the group consisting of:

-imidazoyl, 3-pyridyl, 4-pyridyl, and 3-trifluoromethyldichlorophenyl, 2-fluorophenyl, 4-methylphenyl, phenyl, amidinophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-(i) 3-aminophenyl, 3-amidinophenyl, 4-2-pyridyl;

(ii) hydrido, ethyl, 2-propenyl, 2-propynyl, propyl, tert-butyl, isobutyl, 1-pentyl, 3-pentyl, 2-methylbutyl, 2,2,2-trifluoroethyl, 6-amidocarbonylhexyl, 4-methyl-2methoxyethyl, 2-methyl-2-butyl, 3-methyl-2-butyl, 2-(sopropyl, butyl, 2-butyl, (R)-2-butyl, (S)-2-butyl, pentyl, 3-hydroxypropyl, 1-methoxy-2-propyl, 2-

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guanidinopropyl, 4-guanidinobutyl, 3-hydroxypropyl, 4dimethylaminopropyl, 2-cyanoethyl, 6-hydroxyhexyl, 2hydroxybutyl, 6-cyanohexyl, 2-dimethylaminoethyl, 3hydroxyethyl, 2-amidinoethyl, 2-guanidinoethyl, 3methylbutyl, 2-methylbutyl, (S)-2-methylbutyl, 3aminopropyl, 2-hexyl, and 4-aminobutyl; and

cyclopropyl, cyclobutyl, cyclopentyl, oxetan-3-y1, azetidin-1-y1, azetidin-2-y1, azetidin-3-y1, cyclohexyl, oxalan-2-yl, 2-(2R)-bicyclo[2.2.1]-heptyl, and 1-piperidinyl; (iii)

A is selected from the group consisting of a bond, CH,, CH,CH, and CH,CH,CH,;

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Ja is C-X';

Jb is C-R1;

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X° is selected from the group consisting of hydrido, hydroxy, hydroxymethyl, amino, aminomethyl, cyano, methyl, trifluoromethyl, and fluoro;

R1 is selected from the group consisting of hydrido, hydroxy, hydroxymethyl, amino, aminomethyl, cyano, methyl, trifluoromethyl, and fluoro;

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chlorobenzyl) amidocarbonyl) phenyl, 3-amino-5-(N-(3-R2 is selected from the group consisting of 3benzylamidocarbonyl)phenyl, 3-amino-5-(N-(2amidocarbonyl-5-aminophenyl, 3-amino-5-(N-

trifluoromethylbenzyl)amidocarbonyl)phenyl, 3-amino-5-(Nmethyl-1-phenylethyl)amidocarbonyl)phenyl, 3-amino-5-(N-(1-phenylethyl) amidocarbonyl) phenyl, 3-amino-5-(N-(1fluorobenzyl)amidocarbonyl)phenyl, 3-amino-5-(N-(2-25

benzylamidosulfonyl)phenyl, 3-amino-5-(N-(2-

chlorobenzyl) amidosulfonyl) phenyl, 3-amino-5-(Nisobutylamidocarbonyl)phenyl, 3-amino-5-(N-(2isopropylamidocarbonyl) phenyl, 3-amino-5-(Npropylamidocarbonyl)phenyl, 3-amino-5-(Nethylamidocarbonyl)phenyl, 3-amino-5-(N-30

cyclobutylamidocarbonyl)phenyl, 3-amino-5-(Nbutyl) amidocarbonyl) phenyl, 3-amino-5-(N-

cyclopentylamidocarbonyl)phenyl, 3-amino-5-(N-cyclohexylamidocarbonyl)phenyl, 3-aminophenyl, 3-carboxy-5-aminophenyl, 3-chlorophenyl, 3,5-diaminophenyl, 3-minophenyl, 3-mithylaminophenyl, 3-methylaminophenyl, 3-methylaminophenyl, 2-methylphenyl, 3-methylaminophenyl, 3-trifluoroacetamidophenyl, 3-bromo-2-thienyl, 2-trifluoroacetamidophenyl, 3-bromo-2-thienyl, 2-thienyl,

yar is selected from the group consisting of 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, 5-guanidino-1-oxo-1-(4-thiazolyl)-2-pentyl, 5-guanidino-1-oxo-1-(5-thiazolyl)-2-pentyl, 5-guanidino-1-oxo-1-(4-amino-2-thiazolyl)-2-pentyl, and 5-guanidino-1-oxo-1-phenyl-2-pentyl.

and 3-thienyl;

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102. The compound of claim 98 wherein the compound is selected from the group consisting of:

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or a pharmaceutically acceptable salt thereof, wherein;
R² is 3-aminophenyl, B is phenyl, A is CH₂CH₂, Y^{AT} is
5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R² is
aminomethyl, and X² is chloxo;

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R² is 3,5-diaminophenyl, B is phenyl, A is CH₂CH₂, Y^{MT} is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R² is aminomethyl, and X² is chloro;

CH₂CH₃, Y^{AT} is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl,

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R' 19 3-carboxy-5-aminophenyl, B is phenyl, A is

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R' is aminomethyl, and X° is chloro;

R² is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is phenyl, A is CH₂CH₂, Y^M is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R¹ is aminomethyl, and X° is chloro;

 R^2 is 3,5-diaminophenyl, B is isopropyl, A is single bond, Y^{AT} is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R is aminomethyl, and X° is chloro;

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R² is 3-carboxy-5-aminophenyl, B is isopropyl, A is single bond, Y^{MT} is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R¹ is aminomethyl, and X^o is chloro;

2

 R^2 is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is isopropyl, A is single bond, Y^{AT} is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R^1 is aminomethyl, and X^0 is chloro;

 R^2 is 3,5-diaminophenyl, B is cyclobutyl, A is single bond, Y^{AT} is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R^1 is aminomethyl, and X° is chloro;

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R² is 3-carboxy-5-aminophenyl, B is cyclobutyl, A is single bond, Y^{M*} is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R² is aminomethyl, and X° is chloro;

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R² is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is cyclobutyl, A is single bond, Y^{AT} is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R¹ is aminomethyl, and X² is chloro;

R² is 3-aminophenyl, B is phenyl, A is CH₂CH₃, Y^{M*} is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R¹ is chloro, and X° is hydrido;

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 R^2 is 3,5-diaminophenyl, B is phenyl, A is CH_2CH_3 , Y^{MF} is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R^1 is chloro, and X° is hydrido,

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R' is 3-carboxy-5-aminophenyl, B is phenyl, A is CH,CH, YM is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R' is chloro, and X° is hydrido;

R² is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is phenyl, A is CH_CH₂, Y^M is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R¹ is chloro, and X⁰ is hydrido;

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 R^2 is 3,5-diaminophenyl, B is isopropyl, A is single bond, γ^{AT} is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R^1 is chloro, and X° is hydrido,

R² is 3-carboxy-5-aminophenyl, B is isopropyl, A is single bond, Y^{MT} is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R¹ is chloro, and X° is hydrido;

'n

 R^2 is 3-amino-5-(N-benzylamidocarbonyl) phenyl, B is isopropyl, A is single bond, Y^{AT} is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R^1 is chloro, and X° is hydrido;

2

R² is 3,5-diaminophenyl, B is cyclobutyl, A is single bond, Y^{AT} is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R¹ is chloro, and X² is hydrido;
R² is 3-carboxy-5-aminophenyl, B is cyclobutyl, A is

gingle bond, Y* is 5-guanidino-1-oxo-1-(2-thiazoly1)-2pentyl, R¹ is chloro, and X° is hydrido;
R² is 3-amino-5-(N-benzylamidocarbonyl)phenyl, B is
cyclobutyl, A is single bond, Y* is 5-guanidino-1-oxo-1-(2-thiazolyl)-2-pentyl, R¹ is chloro, and X° is hydrido.

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103. A composition for inhibiting thrombotic conditions in blood comprising a compound of each of claims 2, 3, 12, 66, 73, 81, 89, 97, or 102 and a pharmaceutically acceptable carrier.

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104. A method for inhibiting thrombotic conditions in blood comprising adding to blood a therapeutically effective amount of the composition of claim 103.

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105. A method for inhibiting formation of blood platelet aggregates in blood comprising adding to blood a therapeutically effective amount of the composition of claim 103.

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106. A method for inhibiting thrombus formation in blood comprising adding to blood a therapeutically

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effective amount of the composition of claim 103.

107. A method for treating or preventing venuous thromboembolism and pulmonary embolism in a mammal comprising administering to the mammal a therapeutically effective amount of the composition of claim 103.

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108. A method for treating or preventing deep vein thrombosis in a mammal comprising administering to the mammal a therapeutically effective amount of the composition of claim 103.

109. A method for treating or preventing cardiogenic thromboembolism in a mammal comprising administering to the mammal a therapeutically effective amount of the composition of claim 103.

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110. A method for treating or preventing thromboembolic stroke in humans and other mammals comprising administering to the mammal a therapeutically effective amount of the composition of claim 103.

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111. A method for treating or preventing thrombosis associated with cancer and cancer chemotherapy in humans and other mammals comprising administering to the mammal a therapeutically effective amount of the composition of claim 103.

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112. A method for treating or preventing unstable angina in humans and other mammals comprising administering to the mammal a therapeutically effective amount of the composition of claim 103.

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113. A method for inhibiting thrombus formation in blood comprising adding to blood a therapeutically effective amount of a compound of each of claims 2, 3,

12, 66, 73, 81, 89, 97, or 102 with a therapeutically effective amount of fibrinogen receptor antagonist.

114. A compound having the structure:

 $X_1,\ X_2,\ X_3,\$ and X_6 are members of a heterocyclic or aromatic core ring, wherein

 \boldsymbol{X}_s and \boldsymbol{X}_t are independently carbon, nitrogen, oxygen \boldsymbol{X}_1 and \boldsymbol{X}_2 are independently carbon or nitrogen,

or sulfur, provided when X_5 is carbon it is -CH=, -C(F)=

-C(Br)=;

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 T_3 is hydroxy, alkoxy, substituted alkoxy, or substituted amino;

 $\mathbf{z}_{\mathbf{z}}$ is a hydrogen bond acceptor covalently or datively $\mathbf{z}_{_{1}}$ is hydrocarbyl, or substituted hydrocarbyl; and T_{4} is -Cl, -Br, -I, -S(CH₃₎, or -OSO₂(CF₃);

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bonded to X2.

115. A compound having the structure:

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 $X_1,\ X_2,\ X_5,\ and\ X_6$ are members of a heterocyclic or wherein

aromatic core ring,

 χ_{s} and χ_{s} are independently carbon, nitrogen, oxygen or sulfur, provided when $X_{\rm s}$ is carbon it is -CH=, -C(F)= X_1 and X_2 are independently carbon or nitrogen,

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-C(Br)=;

 $\mathbf{z}_{_{\boldsymbol{k}}}$ comprises hydrocarbyl, substituted hydrocarbyl or carboxylic ring of \mathbf{Z}_{i} being carbon, nitrogen, oxygen, or a 5 or 6 membered heterocyclic or carbocyclic ring, the ring atoms of the 5 or 6 membered heterocyclic or

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 \mathbf{Z}_2 is a hydrogen bond acceptor covalently or datively \mathbf{z}_i is hydrocarbyl, or substituted hydrocarbyl; and sulfur;

bonded to X2.

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116. A compound having the structure:

Wherein

 $Z_1,\ Z_2,\ Z_3,\ Z_4,\ L_3,\ X_1,\ X_2,\ X_3,\ X_4,\ and\ X_5\ are\ as\ defined in claim 1;$

X, is independently carbon or nitrogen;

 X_{ν} and X_{0} are independently a covalent bond, carbon, nitrogen, oxygen or sulfur,

 $X_{\rm p}$ is carbon substituted with a methylene group or carbon substituted with an ethylene group wherein said methylene or ethylene group covalently links $X_{\rm p}$ and $Z_{\rm 1};$

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n is 0 to 2; and $R_{\rm P0}$ and $R_{\rm P0}$ are independently selected from the group consisting of hydrogen, halogen, amino, hydrocarbyl, substituted hydrocarbyl, aryl, wherein aryl is phenyl either unsubstituted or substituted with hydroxy, amino, C1-C6 alkyl, C3-C8 cycloalkyl, or halogen provided that $R_{\rm P0}$ is not present when $X_{\rm P}$ is a bond and $R_{\rm P0}$ is not present when $X_{\rm P}$ is a bond; or $R_{\rm P0}$ along with the ring atoms to which each is attached, form a 5 or 6 membered saturated ring.

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117. A compound having the structure:

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wherein

 $Z_1,\ Z_2,\ Z_3,\ Z_4,\ X_1,\ X_2,\ X_3,\ X_4,\ and\ X_5\ are\ as\ defined\ in$ claim 1,

X, is independently carbon or nitrogen;

 X_{ν} and X_{0} are independently a covalent bond, carbon, nitrogen, oxygen or sulfur,

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 X_{9} is carbon substituted with a methylene group or carbon substituted with an ethylene group wherein said methylene or ethylene group covalently links X_{9} and $Z_{1,1}$

n is 0 to 2; and

R,0 and R,0 are independently selected from the group consisting of hydrogen, halogen, amino, hydrocarbyl, substituted hydrocarbyl, aryl, wherein aryl is phenyl either unsubstituted or substituted with hydroxy, amino, C1-C6 alkyl, C3-C8 cycloalkyl, or halogen provided that R,0 is not present when X, is a bond and R,0 is not present when X, is a bond; or R,0 and R,0, along with the ring atoms to which each is attached, form a 5 or 6 membered saturated ring.